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NCI TO FUND APPROXIMATELY 850 COMPETING GRANTS IN FISCAL 1986 UNDER LATEST BUDGET PROJECTIONS

NCI will fund approximately 850 competing grants this year under President Reagan's proposed rescission and budgetary cuts mandated by the Gramm-Rudman-Hollings balanced budget legislation, NCI Director Vincent DeVita told the Div. of Cancer Etiology's Board of Scientific Counselors. The new funding level will probably result in a

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In Brief

NCI TO GO ALONG WITH NCAB ON KEEPING CLINICAL EDUCATION PROGRAM ALIVE; CAL BALDWIN RETIRES

NCI WILL go along with the National Cancer Advisory Board's recommendation to keep the Clinical Education Program alive, reversing a decision by the Institute's Executive Committee to phase it out. NCAB members and the American Assn. for Cancer Education had asked that at least a minimum level be maintained. The program had been scheduled to receive $4.7 million in FY 1986 (up from $3.9 million in 1985) before the Gramm-Rudman-Hollings 4.3% cut. The Executive Committee will attempt to determine how much the program can be cut this year, which depends largely on funding requirements of the noncompeting renewals, and whether any new applications will be funded in 1986 and 1987. It is unlikely that the new level, at least for the next two to three years, will exceed $1 million a year. . . . **CONGRESSIONAL APPROPRIATIONS** hearings start next week, with NCI Director Vincent DeVita scheduled to testify March 5 before the Senate HHS Appropriations Subcommittee chaired by Lowell Weicker (R-Conn.). The hearing will start with NIH at 9:30 a.m., with DeVita to follow later that day, in the Dirksen Bldg, Rm 116. He will testify before the House HHS Appropriations Subcommittee chaired by William Natcher (D-Ky.) March 11, 10 a.m., Rayburn Bldg 2358. **CALVIN BALDWIN**, executive officer of NCI for 10 years, has retired from his position as NIH associate director for administration. His 37 years of federal service included 33 at NIH. As NCI's chief administrative officer during the 1970s, Baldwin played a major role in implementing the National Cancer Act of 1971 and dealing with the budget and management problems that followed. . . . **NEW APPOINTMENTS** of staff members announced by Univ. of Texas System Cancer Center/M.D. Anderson Hospital: Margaret Kripke to the Vivian L. Smith Chair in Immunology; Isaiah Fidler to the R.E. Smith Chair in Cell Biology; Louise Strong, reappointed to the Sue and Radcliffe Killam Professorship; Jose Trujillo to the Olla S. Stribling Chair; Bernard Levin to the Robert R. Herring Professorship in Clinical Research; Alando Ballantyne to the Ashbel Smith Professorship; and Stuart Zimmerman to the Kathryn O'Connor Research Professorship.

GRANTS PAYLINE EXPECTED TO REACH 160 IN BOTH FISCAL 1986 AND 1987

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priority score payline of about 160, with an overall 27% funding of approved grant applications this year. Under Congress' original appropriations level for NCI in fiscal 1986, the Institute would have funded 924 competing awards. That number will drop to approximately 874 in FY 1987 under the administration's budget proposal, he said. The priority score payline would be similar to that predicted for the current fiscal year.

DCE expects an increase of about $12.5 million in grants funding in FY 1986, up 8.79% to $154.6 million over last year's $142.2 million, division Director Richard Adamson told the board. The division's biggest cut this year will be in cooperative agreements, which will receive an estimated 13.9% decrease in funds from $5.149 million in FY 1985 to $4.431 million in FY 1986. Contracts in the division will be cut 6.81% to $34.879 million in FY 1986 as compared to fiscal 1985's funding level of $37.429 million. The contracts figures do include an increase in Small Business Innovative Research resource contracts from $463,000 in FY 1985 to an estimated $1.257 million in fiscal 1986.

RFAs will increase 2% to $10.857 million over last year's $10.639 million. DCE in house research will receive a 3.38% cut to $40.267 million from FY 1985's level of $41.676 million. Under the current budget estimate, the division's total budget will increase 3.39% to $245.097 million in FY 1986 from $237.056 million in fiscal 1985, an increase of approximately $8 million.

SHUTTLE VECTOR TECHNOLOGY STUDIES CONCEPT APPROVED BY DCE BOARD

NCI's Div. of Cancer Etiology's Board of Scientific Counselors has approved a concept for grant supported research on the application of shuttle vectors and related technology to study the mechanism of DNA damage, repair, and cell sensitivity to ionizing radiation. Proposed first year funding for the three year award is $500,000.

The goal of the award is to encourage research utilizing shuttle vectors and related technology to devise techniques and approaches to measure quantitatively mammalian cell responses to DNA damaging agents, especially ionizing radiation when used individually or in combination with other agents. Emphasis is placed on sensitive quantification of various specific lesions (e.g., base substitutions, normal human fibroblasts and cells from patients with various radiation sensitive syndromes.

Objectives of the award "would include but not be limited to" the use of shuttle vectors and related technology as follows:

(1) To determine the damage to shuttle vector marker genes when they are irradiated inside or outside of the cell and in the presence or absence of agents that alter the physicochemical response to radiation.

(2) To measure the dependence of damage/repair processes on dose, dose protraction, and radiation quality (e.g., x-rays, gamma rays, neutrons, and other high LET radiations), or the combined effects of ionizing radiation with other agents such as promoters, other chemicals, or non ionizing radiation.

(3) To devise methods to distinquish between mutations arising at the point of DNA damage from mutations that arise in initially undamaged areas of DNA as a consequence of DNA damage elsewhere in the genome.

(4) To investigate physiologic and genetic factors of host cells that influence mutagenesis or transformation such as host cells that have a genetic susceptibility or resistance to radiation or cancer proneness.

Techniques for studying the mechanisms of cellular responses for preventing and for coping with radiation damage to DNA generally include such measurements as DNA single and double strand breaks and repairs, chromosomal abberations and repair, cell survival, mutagenesis and transformation. However, these approaches generally lack specificity at the level of DNA code damage, specific sequence deletion or alteration, and other more subtle kinds of alterations such as chromatin structural changes. Quantitative information at the molecular level is needed to define adequately and to evaluate the biological effects resulting from exposure to low levels of radiation. Accordingly new techiques need to be developed and applied.

Recent developments in recombinant DNA technology, particularly advances in shuttle vector plasmids, should lead to the acquisition of more specific information regarding the location, type and extent of ionizing radiation damage. Because chimaeric plasmids are constructed so that they can replicate in both bacteria and mammalian cells, x-ray treated plasmids introduced into mammalian cells after the irradiation, or the irradiation of cells already containing vectors, can be allowed to respond to the damage. Alternatively, the time course of damage expression or repair of damage specific to DNA can be analyzed by recovery of the plasmid from the mammalian cell and its introduction into the appropriate bacterial system. Bacterial colonies with mutations in marker genes can then be identified and quantitated using

sensitive microbiological assays and the relevant DNA sequences determined to localize and to characterize the mutation.

The recent development of a number of vector systems now makes this approach feasible. These systems include (1) a lambda phage construction (lambda supF-neo vector) that allows analysis of damage to a small marker gene while it is integrated into the chromosomal DNA of the cell; (2) several vectors such as lacI/293 and pZ189 that allow treatment of the target DNA either within the cell after transfection or treatment before transfection; (3) various vector constructions and systems that analyze selected types of mutations or DNA rearrangements (recombination, frameshift, substitution, etc.); (4) a stable autonomously replicating minireplicon derived from EBV and containing the lacI marker gene which has a very low spontaneous mutation rate and high sensitivity to mutagenic agents.

Research with some of these systems has yielded impressive results analyzing mutations induced by ultraviolet light and by chemicals in both repair proficient and nucleotide excision repair deficient cells. However, since a major lesion caused by ionizing radiation is deletion of DNA, the problem of whether or not technical adaptation may be necessary should be considered because of limitations on the deletion size that can be studied; exploratory experiments using X irradiation indicate this problem is not a severe limitation and that vectors can be constructed that can be used to study deletions many thousands of base pairs long.

The combination of lesion specificity and quantitation will advance knowledge about the specific mechanisms of radiation induced damage and repair, and the relationship of such processes to cell killing, mutation, developmental changes, and neoplastic transformation. These techniques could also be instrumental in uncovering the specific defects involved in the various human syndromes that exhibit radiation sensitivity (both ionizing and non ionzing) and/or cancer proneness, e.g., ataxia telangiectasia, retinoblastoma, Huntington's disease, etc.

NCI ADVISORY GROUP, OTHER CANCER MEETINGS FOR MARCH, APRIL, FUTURE

Cancer Clinical Investigation Review Committee—March 3-5, NIH Bldg 31 Rm 10, open March 3 8:30-9 a.m.

American Society of Preventive Oncology—March 5-7, Hyatt Hotel, Bethesda, Md. Annual meeting. Contact Richard Love, M.D., ASPO, 1300 University Ave., 7C, Madison, WI 53706, phone 608-263-7066.

Nonoccupational Exposure to Asbestos in Schools and Other Buildings—March 6-7, Baltimore. Contact Dr. Jacqueline Corn, Dept. of Environmental Health Sciences, Johns Hopkins School of Hygiene and Public Health, 615 N. Wolfe St., Rm 1101, Baltimore 21205, phone 301-955-2609.

Monoclonal Antibody Immunoconjugates for Cancer—March 6-8, Hotel Inter-Continental, San Diego. International conference. Contact Cynthia Saxe, Continuing Medical Education, M-017, Univ. of California (San Diego), La Jolla 92093, phone 619-452-3940.

Damaged DNA--Its Structure and Recognition--March 6-7, Univ. of North Carolina, Chapel Hill. Contact Pam Upchurch, Lineberger Cancer Research Center, School of Medicine, UNC-CH, Chapel Hill 27514, phone 919-966-3036.

Advances in Clinical Oncology--March 8-15, Cottonwood Conference Center, Snowbird, UT. Contact Mary Humphrey, Conference Coordinator, Arizona Cancer Center, Tucson 85724, phone 602-626-6044.

Membrane Mediated Cytotoxicity—March 9-16, Park City, UT. Contact UCLA Symposia, Molecular Biology Institute, Los Angeles 90024, phone 213-206-6292.

1986 Fundamental Tumor Registry Operations Programs—Sponsored by the American College of Surgeons Cancer Dept. March 12-15, Fort Worth, Texas, St. Joseph's Hospital. Contact Margaret Aguilar, local coordinator, phone 817-336-9371; March 17-20, Atlanta, St. Joseph's Hospital, Patty Winters, coordinator, phone 404-876-7535.

Breast Disease Update--March 12-16, Lake Buena Vista, FL. Contact Mount Sinai Medical Center, 4300 Alton Rd., Miami Beach 33140, phone 305-674-2311.

Cancer Chemotherapy: Guidelines and Recommendations for Nursing Education and Practice--March 13, La Mansion del Rio Hotel, San Antonio; and March 14, Doubletree Hotel, Denver. Contact Oncology Nursing Society, 3111 Banksville Rd., Suite 200, Pittsburgh, PA 15216, phone 412-344-3899. 200, Pittsburgh, PA 15216, phone

Nutrition in Practice: Focus on Cancer--March 15, Reno. Contact Barbara Scott, MPH, RD, Nutrition Education & Research Program, Dept. of Family & Community Medicine, Edna Brigham medical Sciences Bldg, Univ. of Nevada, Reno 89557, phone 702-784-6180.

Cancer Centers Support Grant Review Committee--March 20-21, Holiday Inn Crown Plaza, Rockville, Md., open March 20 8:30-9:30 a.m.

Leukemia Society of America--March 20-22, Saddlebrook, Wesley Chapel, Tampa, FL. Second national medical meeting. Contact Louise Toglia, Medical Programs Dept., 733 Third Ave., New York 10017, Phone 212-573-8484.

Current Approaches in Radiation Oncology, Biology and Physics—March 26-28, San Francisco. Contact Seminar Headquarters, Dept. of Radiation Oncology, Univ. of California, San Francisco 94117, phone 800-222-8882, or 415-595-2704.

Oncology Ethics 1986--March 26, Hyatt Regency Hotel, Flint, Mich. Contact Greater Flint Area Hospital Assembly's CHOP, 806 Turri Place, Flint 48503.

Cancer Preclinical Program Project Review Com-

mittee—March 27-28, Marriott Hotel, Bethesda. Open March 27, 8:30-9:15 a.m.

Clinical Cancer Program Project Review Committee—March 27-28, NIH Bldg 31 Rm 4, open March 27, 8:30-9 a.m.

The War on Cancer: 15 Years of Progress--April 2-6, Hyatt Regency Washington on Capitol Hill, Washington D.C. 12th national meeting. Contact ACCC, 12th National Meeting, 11600 Nebel St. Suite 201, Rockville, MD 20852, phone 301-984-9496.

National Council on Radiation Protection & Measurements—April 2-3, Washington. 22nd annual meeting. Contact NCRP, 7910 Woodmont Ave. Suite 1016, Bethesda, MD 20814, phone 301-657-2652.

Diagnosis and Treatment of Neoplastic Disorders--April 3-4, Johns Hopkins Medical Institutions, Baltimore. Contact Diane Heydinger, Program Coordinator, Office of Continuing Education, Johns Hopkins, Turner 22, 720 Rutland Ave., Baltimore 21205, phone 301-955-6046.

Head & Neck Cancer: Strategies for Cure--April 3-4, Westin Hotel, Detroit. Scientific and clinical perspectives. Contact Div. of Continuing Medical Education, Wayne State Univ. School of Medicine, 4201 St. Antoine, 4-H, Detroit 48201, phone 313-577-1180.

Gastrointestinal Oncology 1986—April 3-4, New York. Contact CME Conference Planning Office, C-180, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212-794-6754.

American Radium Society—April 6-10, San Francisco. 68th annual meeting. Contact Suzanne Bohn, ARS, 925 Chestnut St., Philadelphia 19107, phone 215-574-3179.

Interferons as Cell Growth Inhibitors and Antitumor Factors—April 6-12, Steamboat Springs, CO. Contact UCLA Symposia, Molecular Biology Institute, Los Angeles 90024, phone 213-206-6292.

National Conference on Urologic Cancer—April 9-11, Adams Mark Hotel, Philadelphia. Contact American Cancer Society, 90 Park Ave., New York 10016.

Central Cancer Registry Operation--April 10-12, Chicago. First national conference. Contact Cancer Dept., American College of Surgeons, 55 E. Erie St., Chicago 60611, phone 312-664-4050.

New Concepts in Breast Cancer Management—April 12, Cleveland. Contact Barbara Guy, Lowman 211, University Hospitals of Cleveland, 2074 Abington Rd., Cleveland 44106, phone 216-844-7856.

Recent Advances in Bone Marrow Transplantation--April 13-18, Keystone, CO. Contact UCLA Symposia, Molecular Biology Institute, Los Angeles 90024, phone 213-206-6292.

American Roentgen Ray Society—April 13-18, Sheraton Washington Hotel, Washington DC. 86th annual meeting. Scientific program includes presentations on magnetic resonance imaging, GI imaging, uroradiology, mammography, skeletal radiology and neuroradiology. Contact ARRS, 1891 Preston White Dr., Reston, VA 22091, phone 703-648-8900.

In Vitro Toxicology: Approaches to Validation--April 14-15, Baltimore. Johns Hopkins Center for Alternatives to Animal Testing. Contact Program Coordin- ator, Office of Continuing Education, Johns Hopkins School of Hygiene & Public Health, 720 Rutland Ave., Baltimore 21205, phone 301-955-6046.

Biological and Therapeutic Aspects of Cancer Metastasis--April 14-17, Vitoria, Spain. International conference sponsored by the Univ. of the Basque Country. Contact Secretariat, Apartado 1299, 48080 Bilbao, Spain.

Food Antioxidants: International Perspectives--April 21-23, Loew L'Enfant Plaza Hotel, Washington DC. Contact Elaine Auld, International Life Sciences Institute--Nutrition Foundation, 1126 16th St. NW, Washington 20036, phone 202-659-0074.

Cancer Therapeutics Program Project Review Committee—April 21-22, NIH Bldg 31 Rm 6, open April 21 8:30-9 a.m.

Oncology Nursing Center Stage—April 30-May 3, Los Angeles. 11th annual congress. Contact Nancy Berkowitz, Oncology Nursing Society, 3111 Banksville Rd., Suite 200, Pittsburgh PA 15216, phone 412-344-3899.

FUTURE MEETINGS

Advances in Cancer Pain Control--May 30-31, Bunts Auditorium, Cleveland Clinic. Contact Center for CME, Cleveland Clinic Educational Foundation, 9500 Euclid Ave., Rm TT3-301, Cleveland 44106, phone (local) 444-5696; (Ohio) 800-762-8172; (elsewhere) 800-762-8173.

Cancer Nursing: An International Perspective--Sept. 7-12, Hilton Hotel, New York. Fourth international conference. Organized by the International Society of Nurses in Cancer Care in cooperation with Memorial Sloan-Kettering Cancer Center. Contact Secretariat, Conference on Cancer Nursing, 404 Park Ave. South, 9th Floor, New York 10016, phone (outside New York City) 1-800-221-3987.

Molecular Mechanisms in the Regulation of Cell Behavior--Sept. 22-26, Hershey, PA. Contact Executive Director, Tissue Culture Assn., 19110 Montgomery Village Ave., Suite 300, Gaithersburg, MD 20879, phone 301-869-2900.

Urologic Cancer--Sept. 22-24, Westin Hotel, Boston. Postgraduate course sponsored by Harvard Medical School. Contact above, Dept. of Continuing Education, Shattuck St., Boston 02115, phone 617-732-1525.

American College of Epidemiology—Sept. 24-26, New Haven, CT. Annual meeting, scientific symposium, continuing education. Contact Curtis Mettlin, PhD, Secretary, ACE, Roswell Park Memorial Institute, 666 Elm St., Buffalo 14263.

Ninth Annual San Antonio Breast Cancer Symposium—Oct. 31-Nov. 1, San Antonio. Abstracts of proffered papers on the experimental biology, etiology, diagnosis and therapy of breast cancer are invited. Abstract deadline is June 6. Contact Terri Coltman, RN, Cancer Therapy & Research Center, 4450 Medical Dr., San Antonio, TX 78229, phone 512-690-0655.

Current Approaches for the Diagnosis & Treatment of Gastrointestinal Cancers--Nov. 12-14, Hotel Inter-Continental, Houston. Contact Office of Continuing Services, Box 131, M.D. Anderson Hospital & Tumor Institute, 6723 Bertner Ave, Houston 77030, phone 713-792-3030.

RFAs AVAILABLE

RFA 86-CA-08
Title: Studies on the etiology of neoplasia in poikilothermic, aquatic animals: finfish and shellfish

Application receipt date: May 1

A comparatively small number of investigators have generated a large body of information on neoplasms of poikilothermic animals. Studies which initially focused on the description of pathologic characteristics of numerous neoplasms and their species specificity have led to a heightened interest in aquatic animals for bioassay testing, for detection of carcinogens in the environment, and even as comparative oncology models for human cancer.

Tumors have been identified in several species of finfish and shellfish at one or more of the following sites: skin, gill, mantle, oral region, pharynx, stomach, pancreas, liver, kidney, gonads, heart, thyroid gland, nervous system, soft tissues, skeleton, and lymphoreticular and hematopoietic tissues. There are, however, large gaps in our knowledge about how neoplasms in aquatic animals conform to what is known about neoplasms of mammals, their morphologic characteristics, biologic course, relation to host requlating mechanism, and their transplantability and transmissibility.

The purpose of this RFA is to accelerate the development of additional understanding relative to studies on the possible etiology of neoplasia in poikilothermic, aquatic animals: finfish and shellfish. In order to encourage applications from a diverse spectrum of scientists, we have compiled a list of laboratories that have established resources for aquatic animals and whom applicants may wish to contact regarding collaboration, provision of resources, and/or consortial arrangements as appropriate. This list is not necessarily comprehensive and those listed have not given prior consent to be involved in this initiative. It is made available at this time so that interested investigators can begin to establish their own contacts. It is recognized that the expertise and logistics needed for the conduct of meaningful multidisciplinary research rarely resides in a single agency or institution and it will be a focus of this initiative to foster new relationships which seek to encompass the required expertise.

Awards will be made as research project grants and all policies and requirements which normally govern the grant programs of the Public Health Service apply. It should be noted that both nonprofit and for profit institutions, domestic and foreign, may apply. The total project period for applications submitted in response to this RFA should not exceed four years. Each application submitted in response to this RFA will be given dual assignment, to NCI and the National Institute of Environmental Health Sciences. The primary assignment will be determined by mutual agreement of the program directors.

Further information and copies of the complete RFA may be obtained from Dr. David Longfellow, Chief, Chemical & Physical Carcinogenesis Branch, Div. of Cancer Etiology, NCI, Landow Bldg Rm 9B-01, Bethesda, Md. 20892, phone 301-496-5471. Written or telephone inquiries are encouraged.

The concept from which this RFA was derived was approved by the DCE Board of Scientific Counselors last year and was reported in **The Cancer Letter** May 24, 1985, page 5.

RFA 86-CA-07
Title: The transformation mechanisms of human polyomaviruses

Application receipt date: July 15

The Biological Carcinogenesis Program of the Div. of Cancer Etiology is inviting grant applications to elucidate the molecular mechanisms by which human polyomaviruses, e.g. JC virus and BK virus, transform human and animal cells in vitro and in vivo. The major emphasis of research will be in two areas: basic studies on the mechanisms of transformation of human polyomaviruses and their possible role in the etiology of human cancer. Applications may be submitted in either or both of these areas. The scope of this RFA includes both known human polyomaviruses, BK and JC viruses. Applications may propose studies focused on one or both of these viruses. In addition the scope of these studies may be expanded, where appropriate, to include new human polyomaviruses which may be isolated.

Examples of pertinent studies (which are not all encompassing) are: (1) characterization of the viral enhancer/origin sequences and the proteins and genes with which they interact; determination of the significance for transformation of the hypervariability of these sequences and other regions found in natural variants of these viruses; (2) characterization of the viral tumor antigen proteins, particularly with regard to defining functionally and immunologically distinct domains within the proteins; (3) development and utilization of modified human cell lines which can be efficiently transformed by these polyomaviruses or can support high titer lytic growth; development of such cell lines could also help delineate the cofactors needed to produce transformation in vivo; (4) studies of the incidence, integration state, and sequence structure of polyomavirus DNA in normal human tissues and human tumors, particularly tumors which are histologically similar to tumors induced by these viruses in animals; (5) functional analysis of polyomavirus DNA activity in transfection assays and the maintenance of viral sequences upon serial passage of tumor cells in culture; (6) studies of the mechanism of persistent polyomaviral infections in man and the identification of the transformed target cells involved in this interaction.

As a subsidiary to these studies (particularly No. 4 and 5 above) the isolation and characterization of new human polyomaviruses with oncogenic potential is encouraged. In this regard, the putative B-lymphotropic virus described in the scientific literature is a candidate for isolation and characterization.

The total project period for applications submitted in response to this RFA should not exceed five years. Approximately $600,000 will be set aside to specifically fund these applications. The earliest feasible start date for the initial awards will be March, 1987.

Copies of the complete RFA and further information are available from Dr. Alan Schreier, Program Director, DNA Virus Studies II, Div. of Cancer Etiology, NCI, Landow Bldg Rm 9A-22, Bethesda, MD 20892, phone 301-496-1953. Inquiries are encouraged.

The concept from which this RFA was derived was approved by the DCE Board of Scientific Counselors last fall and reported in **The Cancer Letter** Nov. 1, page 4.

PROGRAM ANNOUNCEMENTS

Title: Biological role of exocyclic nucleic acid derivatives in carcinogenesis.

Application receipt dates: June 1, Oct. 1, Feb. 1

The Div. of Cancer Etiology invites grant applications for basic studies that are focused on providing insights and approaches to an understanding of the biological role of exocyclic nucleic acid derivatives in carcinogenesis.

It is the intent of this program announcement to encourage basic mechanistic studies focused on determining the formation, repair and relevance to mutagenesis and carcinogenesis of exocyclic nucleic acid derivatives. It is not intended to make or imply any delimitation to the research supported by the Chemical & Physical Carcinogenesis Program of DCE.

The compounds of interest which are known or are likely to form exocyclic nucleic acid derivatives include vinyl halides (vinyl chloride, vinyl bromide), alkyl carbamates (ethyl and vinyl carbamate), halonitrosoureas (BCNU, CCNU), monofunctional unsaturated aldehydes (acrolein, corotonaldehyde), bifunctional aldehydes (glyoxal, malonaldehyde, glycidaldehyde), beta-propiolactone, acrylonitrile, N-nitrosophyrrolidine and related cyclic notrosamines, and some halogenated ethers and aldehydes (chloro- and bromoacetaldehyde).

Examples of important areas of research emphasis include (1) identification and quantitation of adducts which may be responsible for the carcinogenicity of the test compound in animals, the transformation of cells in culture, or the mutagenicity of the compound in cells in culture or in other test systems; (2) the formation and repair of exocyclic adducts in animals, cells in culture, or test organisms relevant to carcinogenicity, transformation of mutagenicity studies; and (3) the mechanism of mutagenesis or carcinogenesis by exocyclic nucleic acid adducts, or other adducts of biological interest or crosslinks which may be formed by the above mentioned compounds. It is also recognized that there will be a need to develop more sensitive methods to analyze and quantitate the many possible adducts and to detect them in DNA from cells exposed to the chosen compounds. A desired sensitive method, not widely available, is an immunoassay using monoclonal antibodies to the chosen exocyclic adduct or other relevant adduct.

Applications should be submitted on PHS Form 398 and submitted to Application Receipt Office, Div. of Research Grants, NIH, Westwood Bldg Rm 240, Bethesda 20892. A cover letter indicating the application is being submitted in response to this program announcement should be included; a copy of the letter, and requests for additional information should be directed to Dr. Paul Okano, DCE, NCI, Landow Bldg Rm 9C18, Bethesda 20892, phone 301-496-4141.

Title: Characterization of multidrug resistant human and other mammalian tumor cell lines

Application receipt dates: June 1, Oct. 1, Feb. 1

NCI is seeking grant applications for support of research projects to identify and characterize multidrug resistant tumor cells. The development of drug resistance in tumor cell populations treated with chemotherapeutic agents has been recognised as a major problem in cancer treatment. The Div. of Cancer Treatment desires to support research in this area in order to increase the understanding of drug resistance phenomena and develop therapeutic strategies to overcome or circumvent the problem.

This announcement is specifically targeted to stimulate research in the area of multidrug resistance (MDR). Detailed studies in Chinese hamster and murine cell systems have shown that under some selective conditions, e.g., colchicine, vincristine, or adriamycin treatment, cell populations demonstrating a multidrug resistant phenotype emerge. In many of these cells, broad spectrum resistance to multiple agents of different modes of action is associated with reduced intracellular accumulation of drug and the appearance of a membrane glycoprotein marker. Recently, laboratory evidence has been presented that multidrug resistant cells also occur in human tumor cell populations. This latter evidence is consistent with clinical experience, particularly with previously treated patients, wherein resistance to multiple agents of different modes of action is observed.

While some potentially important collateral sensitivities to established antitumor drugs have been observed among mammalian cell types showing the multidrug resistant phenotype, it seems likely that new agents specifically useful in treating these resistant cells will be needed. Development of such agents will require additional insight into the mechanisms of MDR and an adequate number of well characterized multidrug resistant cell lines in which new agents can be studied. This announcement is intended to stimulate applications for grants which propose to develop and characterize multidrug resistant human or mammalian tumor cell lines which have potential for this purpose. The primary emphasis in applications submitted in response to this program announcement should be elucidating the mechanism of resistance in multidrug resistant cell populations.

Multidrug resistant cells may be selected in vitro or derived directly from patients or animals

bearing tumors which have been shown to be resistant to chemotherapy. While the specific approaches and methods for development and characterization of the resistant cells will be left to the applicant, it is suggested that the following areas be addressed in the application: mechanism of multidrug resistance, stability of the drug resistant phenotype, extent of cross resistance, tumorigenicity of the drug resistant cells, and verification of the origin of the cells.

Send applications on Form PHS 398 to the DRG, NIH office listed in the previous announcement. For further information, contact Dr. Mary Wolpert, Developmental Therapeutics Program, DCT, NCI, Landow Bldg Rm 5C03B, Bethesda 20892, phone 301-496-8752.

Title: Mechanisms of site specific metastasis in prostate cancer

Application receipt date: June 1, Oct. 1, Feb. 1

The Organ Systems Program of the Div. of Cancer Prevention & Control seeks applications for studies to develop and evaluate new techniques to predict the metastatic potential of prostate cancer, and to identify steps in the metastatic cascade and characterize the host factors and cellular and molecular properties of prostate cancer cells which determine the incidence and organ distribution patterns of prostate cancer metastasis.

The high mortality rate of prostate cancer may be related to the fact that about 80% of patients first present with evidence of metastasis. A special effort is needed to investigate these peculiar properties of prostate cancer about which, on comparison with other forms of cancer, there is sparse information on the tumor biology of metastasis. In addition, there is a dramatic increase in the incidence of prostate cancer with advancing age.

There is little information on the cellular and molecular events associated with prostate cancer metastasis. New techniques and models are now available to address specific biological questions in a quantitative manner that should provide specific new insight that might impact on the control of this disease.

Recent reports indicate that quantitative pathological techniques may be useful in assessing the aggressive nature of prostatic cancer in man and animal models. These techniques include quantitative pathology, flow cytometry, nuclear morphology, and biochemical indicators. There is a need to mount a systematic study to evaluate these procedures and to determine the biological factors associated with the different tumor types, and to determine the metastatic potential of specific cell types within the heterogeneous cells of a prostate cancer.

Studies on the relationship of cell biology events to metastatic potential are encouraged, e.g. cell motility, lytic enzymes and their inhibitors, cell to cell interactions, and interactions between prostate cancer cells and the extracellular components including the basement membrane and stromal elements.

There is a need to compare paths of metastatic dissemination using both the lymphatic route and the hematogenous route, in order to determine the relative importance of hematogenous dissemination to the liver. Studies are needed to characterize the factors which determine the organ patterns of metastases, including the tertiary spread of prostate cancer. These studies could include cancer cell delivery, numbers of cells delivered and their survival in different organs as well as comparison of metastatic properties of androgen sensitive and insensitive cell lines. Attention might also be directed towards factors responsible for the generation of skeletal lesions which present a particular problem since reports indicate that 55-70% of patients with prostate cancer develop bone metastases. These studies would necessitate the development of new experimental approaches since overt spontaneous skeletal metastases appear to be uncommon in existing animal tumor systems.

Studies are encouraged to determine the biological or pharmacological factors which might regulate the degree or site of metastasis in animal characterized that have different growth properties, routes of metastasis and hormone sensitivity. In addition, human prostatic cancer cells are becoming increasingly available by the acceptability of needle aspiration that is associated with low morbidity.

Submit applications on Form 398 to the DRG address cited in the first program announcement above. Copies of the face page and summary page should be sent to, and further information obtained from, Dr. Andrew Chiarodo, Organ Systems Section, Cancer Centers Branch, DCPC, NCI, Blair Bldg Rm 717, Bethesda 20892, phone 301-427-8818.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, Md. 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-67878-72

Title: Detailed drug evaluation and development of treatment strategies for chemotherapeutic agents

Deadline: May 9

The Developmental Therapeutics Program of the Div. of Cancer Treatment is seeking a contractor to evaluate compounds for anticancer activity in experimental tumor models, including both murine tumors growing in pathogen free immune competent mice and human tumors growing in immune deficient (athymic) mice. Studies will focus on agents identified by the program's in vitro disease oriented drug screen. Experiments will be

designed and conducted to optimize drug activity and evaluate the drug's therapeutic potential. A part of the effort on the project will be devoted to detailed evaluation of selected compounds in cell culture assays. Results from this project will be interrelated with pharmacokinetic, toxicologic and biochemical information to devise and recommend treatment strategies for clinical trial and will be included in investigational new drug applications. Compounds to be studied will be selected and assigned by the government.

As compounds of a commercially confidential nature (discreet) may be evaluated, pharmaceutical and chemical firms will be excluded from the competition. Also, since structural formulas of discreet materials may be provided by the government on occasion, the organization must be willing to sign a confidentiality of information statement.

As a minimum requirement, the organization must have a barrier facility for handling pathogen free immune competent and immune deficient mice. The contractor also shall provide facilities and equipment for animal holding, frozen storage of tumors, tumor transplantation, drug preparation, and treatment; facilities and equipment for the handling of potentially carcinogenic or hazardous materials; and facilities and equipment for propagation and testing human tumor cell lines in vitro.

The principal investigator should have an MD, DVM or PhD in one of the relevant biological sciences (or equivalent experience), should have experience in managing an in vivo screening program utilizing pathogen free or immune deficient mice and in evaluating antitumor agents, should understand the principles of cancer chemotherapy and should devote approximately 20% of her/his time to the project.

It is anticipated that one incrementally funded contract will be awarded for a period of three years. Each increment will be for one year. The contract will be written on a level of effort basis specifying that the contractor is to furnish 16,450 labor hours during each of the three yearly periods.

This effort is currently being performed by Southern Research Institute.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in **The Cancer Letter** Oct. 25, page 5.

Contract Specialist: Jacqueline Ballard
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301-427-8737

RFP NCI-CM-67888-72
Title: Operation of an animal virological diagnostic laboratory
Deadline: Approximately May 9

This competitive acquisition is a 100% set aside for small business with 500 employees or less.

NCI is seeking organizations with the capabilities and facilities for performing viral serological testing on rodents. Serological testing will include the following viruses: PVM, Re03, polyoma sendai, MVM, ectromeilia, M.Ad., LCM, MHV, GD, VII, KRV, H-1, RCV/SDA, SV5, K, and LDHV. It is estimated that the total number of viral serological tests to be performed annually will be approximately 95,000.

To be considered for award of a contract, offerors should meet the following criteria: (1) The principal investigator and other key personnel should have experience in rodent viral serological testing; (2) the PI should be generally considered as an expert in viral serological testing and interpretation of testing results; (3) organizational experience in serological testing for rodent viruses should be available.

The present contractor performing this effort is Microbiological Associates.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in **The Cancer Letter** Oct. 25, page 6.

Contract Specialist: Jacqueline Ballard
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RFP NCI-CP-6101267
Title: Support services for clinical epidemiologic studies
Deadline: Approximately April 10

To continue a multifaceted program in the clinical epidemiology of cancer, the assistance of an organization experienced in providing technical (nonprofessional) and managerial support for all phases of NCI projects is sought. Specific assistance is needed for activities which include (1) preparing for data collection; (2) providing forms and personnel for data collection from interviewing, abstracting, and coding; (3) collecting data and coding all information; (4) entering, editing and tabulating data manually and by computer; (5) managing and supervising all support activities to assure quality; and (6) other assistance including reporting progress.

The particular emphasis will be on data collection, preparing and processing and on interacting with other contractors involved with requesting vital records and tracing study subjects.

In general, projects in the study focus on the use of etiologic leads suggested by clinicians and NCI consultations with oncology services. Biological specimen handling and the review of abstraction of medical and vital records is also part of this ongoing effort. Analysis is done by NCI as is the scientific direction for all projects.

Contract Specialist: Nancy Coleman
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