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DCT Board Approves Three New BRMP RFAs For Immunologic Research, $1.5 Million A Year

The Board of Scientific Counselors for NCI's Div. of Cancer Treatment gave concept approval last week to three

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In Brief

NCI Anniversary Party Moved To May 26; Patricia Randall Heads Women Radiologists

NCI'S 50TH anniversary observance, originally scheduled for May 16, has been changed to May 26. Alumni, current staff and invited guests will celebrate the event at the National Naval Medical Center Officers Club in Bethesda from 4-7 p.m. NCI alumni are invited to write for details and reservations to Bayard Morrison MD, Chairman NCI Semicentennial Committee, Bldg. 31 Rm 10A52, NCI, Bethesda 20892, or phone 301/496-6445. . . . **PATRICIA RANDALL**, Syracuse, NY, has been elected president of the American Assn. of Women Radiologists. Other 1987 officers of the 1,000 member organization are Sandra Fernbach, Chicago, president elect; Dixie Aronberg, St. Louis, vice president; Kay Shaffer, Milwaukee, secretary; and Ellann McCrory, Fort Payne, AL, treasurer. . . . **ANNA SKALKA**, head of molecular oncology at the Roche Institute of Molecular Biology, has been appointed vice president for basic science of Fox Chase Cancer Center. Fox Chase President John Durant also announced that Skalka will be director of the Institute for Cancer Research and a senior member of the Center's scientific staff. . . . **NORTHERN CALIFORNIA** Cancer Center is seeking an associate director for cancer control programs. Qualifications include a minimum of five years postdoctoral research experience and an established record of developing successful, peer reviewed cancer control programs. Send resumes to Thomas Davis, MD, NCCC, PO Box 2030, Belmont, CA 94002. . . . **JORDAN GUTTERMAN**, professor of medicine at M.D. Anderson Hospital & Tumor Institute, has been promoted to chairman of the Dept. of Clinical Immunology & Biological Therapy and to the Virginia H. Cockrell Professorship. . . . **CORRECTION**: NCAB member Louis Sullivan voted for the modification of PO1 application review (**The Cancer Letter**, Feb. 13). Also, the suggestions by Board members that selection of review teams be formalized and that the high and low priority scores be dropped were deleted from the motion of approval but will be considered in the final revisions.

RFAs To Explore Biologicals As Protectors, Study Drug Resistance

(Continued from page 1)
new grant supported projects funded by the Biological Response Modifiers Program. The requests for applications each will set aside $500,000 a year, each of which will support three to four grants for up to five years.

Two of the projects will take BRMP somewhat afield from its historic efforts in development of biological anticancer therapeutics. One will explore use of biologicals for protection of bone marrow against effects of chemotherapy and radiation. The other will study multidrug resistance of neoplastic cells by using immunologic methods.

The third RFA is aimed at development of ways to manipulate the suppressor arm of the immune response to enhance immunologic attack on malignant tumors.

BRMP plans to issue the RFAs this spring, with awards to be made by summer, 1988. Staff description of the concept proposals follows:

Protection of bone marrow against the effects of cytotoxic drugs and x-irradiation.

One of the limiting features of cancer treatment using standard cancer chemotherapy and x-irradiation is damage to the bone marrow leading to the absence of peripheral blood and tissue leukocytes necessary for host defense against infectious agents. In addition, such damage to bone marrow causes failure of RBC and platelet production. Recently, cytokines, such as IL-1, G-CSF, GM-CSF, IL-2 and gamma interferon have become available in quantities sufficient for clinical use and, moreover, preliminary studies have indicated that such agents can protect against the detrimental effect of x-irradiation and chemotherapy. For example, a more rapid recovery of peripheral blood neutrophils has been observed in animal systems after the use of GM-CSF. In addition, both G-CSF and GM-CSF appear to increase the neutrophil and macrophage effector function on a per cell basis. The detailed mechanism of action and full potential of these agents are still to be explored.

Goal of this research will be to develop basic preclinical information that will aid in the development of clinical use of these agents. This RFA will, therefore, foster research in animal models to explore these questions. Models in which normal animals or tumor bearing animals are treated with standard anticancer treatment and then treated with lymphokines at various times before and after the standard therapy would provide useful information prior to human use of such strategies. Detailed studies of peripheral blood and organ counts of various hematopoietic cell types would be indicated. Also, colony forming abilities of cells contained within bone marrow and other blood forming organs should be performed.

The above could also be integrated with in vitro models of hematopoiesis, such as Dexter and/or Witte-Whitlock cultures. Such cultures could be employed to study effects of such lymphokines at a cellular and molelcular level on hematopoiesis as well as their effect on stromal cells and their interaction with hematopoietic progenitor cells. Considering that many patients who receive cancer therapy die as a result of infectious disease, the possible beneficial effects of such CSF and other lymphokines on infectious disease could also be studied in the above mentioned animal models.

Also encouraged would be the study of combinations of known lympokines and CSFs, and the discovery of entirely new lymphokines and BRMs that might mediate such effects. The discovery of any defined agent of any kind that could have similar effects would be highly desirable.

Finally, since other rapidly proliferating tissue, such as cells of the gastrointestinal tract, is also damaged by cancer chemotherapy and x-irradiation, the protective effects of the above agents or other agents could be explored in this regard. While exploring mechanisms of protective action, it is extremely important in these proposals that endpoints measuring anticancer effects should also be included.

Board member Robert Schimke raised the question of whether enough research in this area is already going on. "If not, that raises the question of whether this is a drop in the bucket. Also, companies are well aware of these issues and some are in clinical trials."

Board member John Mendelsohn disagreed. "Most companies do not look at this with an integrated approach."

Board Chairman Paul Calabresi also felt that $500,000 a year might not be enough money and he asked for two votes, one on the concept and another on the amount requested. The Board voted to approve both the concept and the dollar request.

Immunologic investigation of multidrug

resistance in neoplastic cells.

The emergence of drug resistant cancer cells during the course of chemotherapy continues to be a major problem. The mechanisms of this resistance are numerous and complex. During the past 10 years, a new system has been defined which, in part, explains a major portion of the drug resistance of cancer cells. This system is termed multidrug cross resistance (MDR). That is, when a tumor cell becomes resistant to one class of drug, the same cell demonstrates resistance to another class of unrelated drugs. This type of resistance has been determined to be due to the increased cell membrane expression of a 170,000 dalton glycoprotein. This membrane protein controls the permeability and efflux of drugs from the cell. Cells having a large amount of this protein are able to expel the drug at a faster rate.

For this reason, this protein has been called the P-glycoprotein (P-170). A cell becomes resistant to drug therapy because, presumably, under drug selection, only those rare cells survive that have large amounts of this protein already expressed on their surface. It should be noted that P-170 may be one member of a family of proteins. The gene for this protein has now been cloned and the amino acid sequence is now known. Transvection of drug sensitive cells with this gene converts them into drug resistant cells.

In part from the known amino acid sequences, some idea of the cell membrane localization and arrangements of various portions of this complex protein can be deduced. There are several intracytoplasmic portions, an intramembranous portion, and a small external domain. Exactly how the presence of increased amounts of P-170 in the cell membrane of resistant cells leads to decreased drug concentration within the cell remains to be fully understood. However, it has been shown by photo affinity labeling that some drugs bind directly to P-170.

The finding of this new protein and its functions raises another series of important questions: What is the normal function of this protein? Does it have a role in protection of cells from harmful chemicals in the environment? Is this the reason that colonic epithelial cells and their malignant counterparts already display some degree of MDR? Does P-170 normally act as an anticarcinogenesis agent? Why don't normal cells of patients also acquire MDR during therapy, or do they to some degree?

Recently, several groups have produced monoclonal antibodies to the P-170. These antibodies can be used to identify cells and tissues bearing increased amounts of P-170. Furthermore, some of these antibodies can affect the function of PL-170.

The goal of this research will be to develop immunologic methods that will lead to a further understanding of how this or similar proteins operate and to develop methods to interfere with the function of P-170 on cancer cells that will lead to favorable clinical effects.

Studies are encouraged which will (1) determine the functional domains of the P-170 by production of monoclonal antibodies to polypeptide from various domains. To test these antibodies for inhibition of growth of multidrug resistant cells; inhibition of drug efflux by cells; inhibition of drug binding to the P-170 molecule resulting in increased intracellular levels of drug. These same antibodies could also be used to study normal functions of this protein.

(2) To then use monoclonal antibodies to inhibit growth of human drug resistant tumor xenografts in a suitable nude mouse model system.

(3) To use monoclonal antibodies to study receptor function of P-170. Here the fate of the drug P-170 conjugate (exocytosis, coated pit localization, breakdown of the conjugate and P-170 recycling) should be examined.

(4) To investigate the details of how other drugs, such as the calcium channel blocking agents (which can partially overcome MDR) interact with P-170 on the cell surface. For example, will some monoclonal antibodies block the association between calcium channel blocking agents and P-170?

(5) To use monoclonal antibodies to see if P-170 molecules exist as a family of molecules each of which may be specific for a different drug.

(6) To use monoclonal antibodies to screen tumor tissues to determine elevated levels of P-170 and correlate with drug resistance in patients. Increased levels might indicate that the type of drug to be used in a particular patient should be switched.

(7) To test P-170 as a target for monoclonal antibody coupled to a toxin or radionuclide for ultimate patient therapy.

(8) To develop T-cell and other types of cell mediated immunity to P-170 bearing cells in in vitro and animal models.

Board member Yung-chi Cheng said that "many labs are working on this. A phenomenal number of abstracts for the AACR meeting have come in on MDR." But DCT Director Bruce Chabner said that there are not a lot of antibodies available for this type of research.

"The best mechanism for this is a contract," Schimke said. Chabner and Carl Pinsky, chief of the Biological Resources Branch, agreed that would be possible, and Pinsky suggested "we could do both, put contractors to work making antibodies."

"We could contact people who have antibodies and ask for them," Chabner said. "If we can't get it, then make it ourselves."

BRMP Director Dan Longo said "We asked four people for their antibodies. We are 0 for four."

The concept was approved as presented.

Manipulation of the suppressor arm of the immune response directed towards successful human immunotherapy.

The cellular immune system is highly complex, being composed of different types of cells located in various central and peripheral lymphoid organs. Other factors such as complement, antibody, and cytokines all interact with these cells in a complex fashion. Another aspect of the immune system is that it is highly regulated so that normal immunological defenses remain within certain limits and do not get out of control. In spite of much recent new knowledge, much remains to be learned.

This complex immunologic network can affect, among other things, the growth of cancer cells. In certain cases, most clearly established in animal models, tumors can be demonstrated to be antigenic and they can be rejected on the basis of immune responses to their antigens. However, this potentially beneficial host response can be inhibited by the development of suppressor functions, which may be present as part of the normal physiologic process by which excessive immune responses are regulated. Thus, a tumor that might otherwise be rejected is not because of this normal inhibitory regulatory system. In fact, it is possible that the development and progression of some cancers may be due to suppression of normal immunologic mechanisms.

In the past few years several groups have demonstrated that the suppressor arm of the immune response can be abolished or diminished with clinically beneficial results in tumor bearing animal models. Moreover, the suppressor lymphocyte subtypes have been identified in several of these animal models. However, as elegant as these studies are, they are nevertheless very difficult to translate into practical therapy for tumor bearing humans. First, it is very hard to establish whether individual tumors in humans are antigenic (it is principally with antigenic tumors that such specific suppressor modulation might be expected to be successful). Second, the detailed mode of action of certain agents, such as cyclophosphamide, which affect the suppressor arm of the immune response, are poorly understood even in animal systems. Third, many of the animal models that demonstrate suppressor cell phenomenon do so by in vivo measurement of progressive tumor growth. Convincing in vitro systems that can measure such suppressor effects in cancer tumor systems are rare. In other systems, such as in vitro suppression of antibody formation, this is possible and putative suppressor substances have been identified. Fourth, in animal models, the inhibition of suppressor cell function has to be performed in a precisely timed manner with regard to the growth of tumor. This would hardly be possible in humans.

Despite all these difficulties, attempts to regulate the suppressor phase of the immune response in humans, so as to achieve a successful antitumor effect, should be a goal to be be reached.

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The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. In the case of RFAs, the amounts cited are the maximum that will be set aside to fund those particular grants, the final amount depending on NCI's budget and program priorities. Responses should be based on workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when NCI is ready to release them.

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New agents that can decrease suppressor cells should be sought. Known examples of such agents now include cyclophosphamide, cimetidine, cyclooxygenase inhibitors and

deoxyguanosine. The cellular and molecular mechanism of action of such agents should be explored. For example, suppressor T-cell subsets appear to be more susceptible than effector T-cell subsets to a number of toxic agents (reasons for this are unclear). Also desirable would be the establishment of innovative animal models to explore the role of suppressor cells in cancer biology. This could include therapy of UV induced and carcinogen induced autochthonous tumors. The proposal should include some experiments which are designed to demonstrate cancer regression in a therapy model.

The Board approved the concept without dissent.

The Board went along with BRMP's request to extend the current master agreements for phase 1 clinical studies for one more year and to increase the amount available for those studies to as much as $4 million.

Pinsky explained that plans to replace the master agreements with full time phase 1 contracts had been placed on hold last year because of uncertainty of funding due to Gramm-Rudman. The master agreements budget had been limited to $1.2 million. It now appears that at least $3 million will be available for BRMP phase 1 trials in FY 1987 and a similar amount for 1988. He asked that the master agreements be extended for a year while the full time phase 1 contracts are being competed. The extra money will support evaluation of monoclonal antibodies, alone or conjugated with radionuclides or toxins; a variety of human cytokines and one or two immunomodulators.

NCI Advisory Group, Other Cancer Meetings For March, April Future

Biennial International Breast Cancer Research Conference--March 1-5, James L. Knight Convention Center, Miami. Contact Dr. Diana Lopez, Conference Chairman, Dept. of Microbiology & Immunology D4-4, Univ. of Miami School of Medicine, PO Box 016960, Miami 33101, phone 305/547-6632.

Seventh Annual DNA/Hybridoma Congress--March 1-4, San Francisco. Contact DNA Hybridoma, Scherago Associates, 1515 Broadway, New York 10036, phone 212/730-1050.

Div. of Cancer Etiology Board of Scientific Counselors--March 5-6, NIH Bldg 31 Rm 10. Closed March 5 9 a.m.-1 p.m., open 1 p.m.-adjournment and, March 6, 9 a.m.-adjournment.

Relationship of Time and Dose in the Radiation Therapy of Cancer: A Frontier Revisited--March 7-8, Sheraton Palace Hotel, San Francisco. 22nd annual San Francisco Cancer Symposium. Contact West Coast Cancer Foundation, 50 Francisco St., Suite 200, San Francisco 94133, phone 415-981-4590.

Anticarcinogenesis and Radioprotection--March 9-12, Gaithersburg, MD. 1987 international conference. Contact Dr. Michael Simic, Center for Radiation Research, National Bureau of Standards, Gaithersburg 20899, phone 301/975-2000.

Fundamental Tumor Registry Operations--March 10-13, Bakersfield, CA. Contact Kathy Shetrone, CTR, Local Coordinator, Regional Cancer & Blood Disease Center of Kern, phone 805/327-5529.

American Society of Preventive Oncology--March 11-13, San Francisco. Annual meeting open to professionals in any clinical, educational or research discipline which contributes to a comprehensive approach to cancer prevention. Contact Richard Love MD, ASPO, 1300 University Ave., 7C, Madison, WI 53706, phone 608/263-6919.

Adjuvant Therapy of Cancer--March 11-14, Tucson Convention Center. Fifth International Conference, sponsored by the Arizona Cancer Center. Contact Mary Humphrey, Conference Coordinator, Arizona Cancer Center, Univ. of Arizona College of Medicine, Tucson 85724, phone 602/626-2276.

Cancer Program Product Line Management--March 11-14, Sheraton Washington Hotel, Washington DC. Assn. of Community Cancer Centers 13th national meeting. Starts with the joint meeting with the Assn. of American Cancer Institutes, "Advances in Cancer Control V," March 11. Contact ACCC, 13th National Meeting, 11600 Nebel St., Suite 201, Rockville, MD 20892, phone 301/984-9496.

Monoclonal Antibody Immunoconjugates for Cancer--March 12-14, Hotel Inter-Continental, San Diego. Second international conference. Contact Cynthia Saxe, Medical Meeting Planner, Univ. of California, La Jolla 92093, phone 619/534-3940.

Oncology Update '87--March 13-14, Sheraton Lakeview Resort and Conference Center, Morgantown, WV. Contact Office of Continuing Education, G-104 Basic Sciences Bldg, West Virginia Univ. School of Medicine, Morgantown 26506, phone 304/293-3937.

Status of Treatment of Metastatic Renal Cell Carcinoma--March 13-14, Vienna. International symposium sponsored by the International Union Against Cancer. Contact Prof. Dr. J. Kuhbock, 2nd Medical Department, Univ. of Vienna, Garnisongasse 13, A-1090 Vienna, Austria.

President's Cancer Panel--March 16, UCLA School of Medicine, School of Nursing Auditorium, Louis Factor Bldg, A-660, Tiverton Dr., corner Circle Dr. South, Los Angeles. Innovations in cancer treatment. Starts at 8:30 a.m., open.

Leukemia Society of America--March 18-21, Town & Country Hotel, San Diego. Third national symposium. Contact LSA Medical Conference, c/o Bostrom Corp., 435 N. Michigan Ave., Suite 1717, Chicago 60611.

Symposium of the German Section of Experimental Cancer Research--March 18-20, Heidelberg. Contact Institute of Medical Virology, Frankfurter-Str 107, 6300 Giessen, FRG.

Human Values and Cancer--March 19-21, San Francisco. Fifth national conference, sponsored by the American Cancer Society. Contact Human Values and Cancer, American Cancer Society, 13 Elm St., Manchester, MA 01944.

Nonoccupational Exposure to Asbestos in Schools and other Buildings: Risk Assessment and Management--March 23-24, 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.

Surgical Management of Metastatic Disease--March 25-27, Memorial Sloan-Kettering Cancer Center. Contact CME Office, C-180 MSKCC, 1275 York Ave., New York 10021, phone 212/794-6754.

Growth Control and Cancer: Molecular Approaches and Clinical Implications--March 26-27, Univ. of North

Carolina, Chapel Hill. Contact Lineberger Cancer Research Center, School of Medicine, UNC, Chapel Hill, NC 27514.

Small Cell Lung Cancer--March 27-28, Ravenna, Italy. International conference. Contact Organizing Secretariat OIC, via G. Modena, 19, 50121 Florence, Italy.

National American Society of Clinical Pathologists and the College of American Pathologists--March 28-April 2, San Francisco. Contact Rita Kamber, College of American Pathologists Meeting Planner, phone 312/966-5700.

American Assn. of Immunologists--March 29, Washington DC. Contact J.F. Saunders, Executive Office, AAI, 9650 Rockville Dr.,Bethesda, MD 20814, phone 301/530-7178.

Cancer Education at the Workplace--March 29-April 1, Helsinki. UICC workshop. Contact Dr. L. Elovaino, Chief, Health Education, Cancer Society of Finland, Liisankatu 218, 00170 Helsinki 17, Finland.

Federation of American Societies for Experimental Biology--March 29-April 3, Washington DC Convention Center and nearby hotels. FASEB's 71st annual meeting, 75th anniversary and centennial celebration of FASEB member American Physiological Society. Nearly 7,000 scientific papers will be presented and more than 300 companies will display exhibits. Contact FASEB, 9650 Rockville Pike, Bethesda, MD 20814, phone 301/530-7075.

Cancer Progress II--March 30-31, Omni Central Hotel, New York. Contact Communitech Market Intelligence Inc., PO Box 67, Yorktown Heights, NY 10598, phone 914/245-7764.

Fundamental Tumor Registry Operations--March 30-April 2, Roanoke, VA. Contact Roanoke Memorial Hospitals, Mooris Reece, Local Coordinator, phone 703/981-7648.

9th Cancer Congress of the GDR--March 30-April 2, Leipzig. Contact Dr. M. Schoenfelder, Organizing Committee, University Clinic of Surgery, Liebigstr, 20A, 7010 Leipzig, GDR.

Cancer Clinical Investigation Review Committee--March 30-31, Omni Georgetown Hotel, Washington DC. Open March 30 8-8:30 a.m.

Home Total Parenteral Nutrition--April 1, Cleveland. Contact Dept. of Continuing Education, Cleveland Clinic Foundation, 9500 Euclid Ave. Rm TT3-301, Cleveland, OH 44106, phone (local) 444-5696; (within Ohio) 800/762-8172; elsewhere, 800/762-8173.

Human Retroviruses, Cancer and AIDS--April 1-6, Keystone, CO. Approaches to prevention and therapy. Contact UCLA Symposia, Molecular Biology Institute, UCLA, Los Angeles 90024, phone 213/206-6292.

Radiology 87--April 1-3, Southampton, UK. All aspects of radiology, including radiation oncology. Contact British Institute of Radiology, 36 Portland Place, London WIN 3DG, UK.

Management of Cancer in Women--April 2-3, Johns Hopkins Medical Institutions. 13th annual symposium on diagnosis and treatment of neoplastic disorders. Contact Program Coordinator, Office of Continuing Education, Johns Hopkins, Turner 22, 720 Rutland Ave., Baltimore 21205, phone 301/955-6046.

The Child With Cancer in the Community--April 2-3, M.D. Anderson Hospital. 12th annual mental health conference. Contact Office of Conference Services, Box 131, M.D. Anderson Hospital & Tumor Institute, 1515 Holcombe Blvd., Houston 77030, phone 713/792-2222.

Cancer Preclinical Program Project Review Committee--April 2-3, NIH Bldg 31 Rm 9, open April 2 8:30-9:15 a.m.

Nursing Management Strategies for Access/Delivery Devices--April 3, Cleveland Clinic, Bunts Auditorium. Contact Dept. of Continuing Education, Cleveland Clinical Educational Foundation, 9500 Euclid Ave. Rm TT3-301, Cleveland, OH 44106.

Immunobiology in Clinical Oncology and Immune Dysfunctions--April 4-7, Nice. Contact S.A. Kay, International Society for Preventive Oncology, 217 E. 85th St., Suite 303, New York 10028, phone 212/534-4991.

British Assn. for Cancer Research--April 5-8, Newcastle. Contact Barbara Cavilla, BACR Secretariat, Institute of Biology, 20 Queensberry Place, London SW7 2DZ, UK.

American Radium Society--April 6-10, Portman Inter-Continental, London. 69th annual meeting. Contact Suzanne Bohn, Executive Secretary, American Radium Society, 925 Chestnut St., Philadelphia 19107, phone 215/574-3179.

Tumor Progression and Metastasis--April 6-12, Keystone, CO. UCLA Symposia.

Tumor Imaging--April 609, Island of San Servolo, Venice. Contact Secretariat, European School of Oncology, Via Venezian 1, 20133 Milano, Italy.

World Conference on Smoking and Health--April 7-10, Kitakyushu, Japan. Contact Japan Heart Foundation, 603 Maru Bldg, 1-4-1 Marunouchi, Chiyoda-ku, Tokyo 100, Japan.

Fundamental Tumor Registry Operations--April 7-10, Our Lady of Mercy Medical Center, Bronx, New York. Contact Frank Corvino, Local Coordinator, phone 212/920-8288.

National Council on Radiation Protection and Measurements--April 8-9, Washington DC. 23rd annual meeting. Contact NCRPM, 7910 Woodmont Ave., Suite 1016, Bethesda, MD 20814, phone 301/657-2652.

Genes and Cancer--April 10, Memphis. Dorothy Snider Foundation Forum on Cancer Research. Contact Dr. James Hamner, Univ. of Tennessee (Memphis), 62 S. Dunlap Suite 507, Memphis 38163, phone 901/528-6354.

Oncology Core Course: 1987--April 13-17, Allentown, PA. Contact Oncology Nurse Education, Comprehensive Community Cancer Center, Allentown Hospital, 17th and Chew Streets, Allentown 18102, phone 215/778-2582.

Cancer Therapeutic Program Project Review Committee--April 16-17, Holiday Inn Crown Plaza, Rockville, MD. Open April 16 8-8:30 a.m.

National Congress of Cancer--April 16-18, Ankara. Contact Assoc. Prof. Dr. Emin Kansu, Turkish Assn. for Cancer Research and Control, Atac Sok No: 21 Yenisehir, Ankara, Turkey.

Prediction of Tumor Treatment Response--April 21-24, Banff Springs Hotel, Banff, Canada. Contact Meg Keiser, American College of Radiology, 925 Chestnut St., Philadelphia 19107, phone 215/574-3153.

Endocurietherapy/Hyperthermia Workshop and Symposium--April 21-24, Memorial Medical Center, Long Beach, CA. Contact Dr. Khalid Sheikh, Dept. of Radiation Oncology, Memorial Medical Center of Long Beach, 2801 Atlantic Ave., Long Beach 90801, phone 213/595-2929 or 595-3873.

Malignant Lymphomas--April 22-23, Cairo. Contact Dr. Mohamed Nabil El-Bolkainy, National Cancer Institute, Kars El-Ainy St., Fom-El-Khaling, Cairo, Egypt.

Realities of Cancer in Minority Communities--April 22-25, Westin Galleria. Houston. First biennial symposium on minorities and cancer. Contact Office of Conference Services, Box 131, M.D. Anderson, 1515 Holcombe Blvd., Houston 77030, phone 713/792-2222.

New Frontiers in Cancer Research--April 23-24, Robert Wood Johnson Medical School, Piscataway, NJ. Sponsored by the New Jersey Commission on Cancer Research. Contact the Commission, 28 W. State St., 7th Floor, Rm 715, CN 360, Trenton, NJ 08625, phone 609/633-6552.

Seminar on the Use of Interferons in Oncology--April 23-24, Milano. Contact European School of Oncology, Via Venezian 1, 20133 Milano, Italy.

Cancer Update: Prevention, Screening, New Treatment Modalities--April 24, Providence Medical Center,

Portland, OR. Contact Diane Gordon, Cancer Center Coordinator, Providence Medical Center, 4805 NE Glisan, Portland 97213, phone 503/230-6014.

Joint Annual Meeting--April 25-30, Grosvenor House, London. Society of Surgical Oncology, Society of Head and Neck Oncology, British Assn. of Surgical Oncology, and Assn. of Head and Neck Oncologists of Great Britain. Contact SSO/SHNS, 13 Elm St., Manchester, MA 01944, phone 617/927-8330.

Carcinogenic and Mutagenic N-Substituted Aryl Compounds--April 25-28, Hyatt Regency Hotel, Dearborn, MI. Third international conference. Contact Charles King PhD, Dept. of Chemical Carcinogenesis, Michigan Cancer Foundation, 110 E. Warren Ave., Detroit 48201, phone 313/833-0710 ext. 383.

New Strategies in the Management of Lung Cancer--April 25, Cleveland. Contact Barbara Guy, Ireland Cancer Center, Lowman Bldg 211, Univ. Hospitals of Cleveland, 2074 Abington Rd., Cleveland, OH 44106, phone 216/844-7856.

American Roentgen Ray Society--April 26-May 1, Fontainebleau Hilton Hotel, Miami Beach. 87th annual meeting. Contact ARRS, 1891 Preston White Dr., Reston, VA 22091.

Advances in Gynecological Oncology--April 26-30, Venice-Lido. Contact Organizing Secretariat, Meeting of Gynecological Oncology, Galleria Storione, 2a, 35123 Padua, Italy.

Nutrition, Growth and Cancer--April 26-30, Athens. Contact Dr. G.P. Tryfiates, Dept. of Biochemistry, West Virginia Univ. School of Medicine, Morgantown 26506, phone 304/293-2494.

International Conference on Radiation Oncology--April 26-30, Shanghai. Contact Shanghai International Conference on Radiation Oncology, Secretariat Office, 270 Dong An Road, Shanghai, China.

Physical Aspects of Hyperthermia--April 27-May 1, Sheraton Univ. Center, Durham, NC. Contact Sandy Huskins, Duke Univ. Medical Center, Box 3085, Durham 27710, phone 919/684-4384.

Diagnostic Cytopathology for Pathologists--April 27-May 8, Johns Hopkins Medical Institutions, Baltimore. Contact John Frost, MD, 604 Pathology Bldg, Johns Hopkins Hospital, Baltimore 21205.

Fundamental Tumor Registry Operations--April 28-May 1, Indianapolis. Contact Laura Shannon, RRA, Local Coordinator, phone 317/929-8288.

Action in the 80s: Meeting the Challenges of a New Era--April 29-May 2, Park Plaza Hotel, Boston. Third annual conference of the National Assn. of Oncology Social Workers and the 11th annual conference of the Assn. of Pediatric Oncology Social Workers. Contact Cynthia Medeiros, LICSW, Dana-Farber Cancer Institute, Social Work Dept., 44 Binney St., Boston 02115 phone 617/732-3459; or Martha Burke, LICSW, Brigham and Women's Hospital, Social Work Dept., 75 Francis St., Boston 02115, phone 617/732-6469

FUTURE MEETINGS

Recent Advances in Cancer Management--Sept. 2-23, Hong Kong. EORTC symposium. Contact ICTS, Vere & Associates Inc., 17/F, Jubilee Commercial Bldg, 42-46 Gloucester Rd, Hong Kong.

International Symposium on Sarcomas--Oct. 8-10, Innisbrook, Tarpon Springs, FL. Contact James Ryan, MD, Dept. of Orthopaedic Surgery, Wayne State Univ. School of Medicine, 4201 St. Antoine 7C, Detroit 48201, phone 313/577-5098.

Scripps Cancer Symposia--Oct. 19-21, Sheraton Harbor Island Hotel, San Diego. 11th annual Cancer Symposium and 7th annual Cancer Symposium for Nurses, sponsored by Scripps Memorial Hospital. Contact Nomi Feldman, Conference Coordinator, 3770 Tansy, San Diego 92121, phone 619/453-6222.

XIIIth International Symposium for Comparative Research on Leukemia and Related Diseases--Nov. 8-13, Laromme Hotel, Jerusalem. Also, post symposium satellite workshops will be held Nov. 14-17 in Eilat, Israel. Contact Dr. David Yohn, Secretary-General, Suite 302, 410 W. 12th Avenue, Columbus, OH 43210.

10th Annual San Antonio Breast Cancer Symposium--Dec. 11-12, San Antonio. Abstracts of proffered papers on the experimental biology, etiology, prevention, diagnosis and therapy of breaast cancer are invited. Contact Terri Coltman, RN, Cancer Therapy & Research Center, 4450 Medical Dr., San Antonio, TX 78229.

RFPs Available

Requests for proposals 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-CN-75424

Title: Preclinical toxicology of chemopreventive agents

Deadline: Approximately May 15

The required services will be defined by master agreement orders issued during the one year period of performance. This is a reissuance of a master agreement announcement and is being reissued with the intention of seeking new sources and enlarging the current pool of master agreement holders.

A primary function of the chemoprevention program is the identification and evaluation of agents for possible utilization in clinical trials in humans. Candidate agents, whether from natural sources or synthesized, have been evaluated for anticancer efficacy in various screening tests. However, before a decision can be made as to their suitability for the phase 1 clinical trials in humans, they must be evaluated for toxicity in animals.

The basic objectives of this project will be to evaluate the acute, subacute/subchronic and chronic toxicity of designated agents. These studies will be performed in animals (rodents and dogs) and will include conventional short term studies, life time studies in rodents and dogs, and multigeneration teratogenecity studies. The agents would be given primarily by the oral route.

A summary of the tasks required in the project are as follows:

Task 1--Perform acute toxicity, pilot dose range finding, and 13 week subchronic toxicity in rats and dogs by the oral route. Include, where appropriate, complete gross necropsies, histopathological examinations, and clinical laboratory studies.

Task 2--Develop a protocol for a pharmacokinetic profile for each investigational agent. The protocol and profile may build upon published data and data provided by the manufacturer of the agent or NCI staff. Additional studies necessary to complete the pharmacokinetic profiles for the rat and the dog shall be performed by the contractor. Pharmacokinetic studies will provide parameters of absorption, blood concentration-time profiles, distribution and excretion. Data on tissue concentration of the test agent, determined as part of the toxicology testing shall contribute to the pharmacokinetic profile. Information on major metabolites shall be included in order to provide as complete a picture as possible of the

overall distribution and fate of the test agent. Appropriate modeling shall be applied to determine probable pattern of distribution and compartmentalization.

The first studies performed shall be designed to provide absorption and half life information necessary to plan the 90 day rat and dog toxicology studies.

Task 3--Develop and perform teratogenicity studies on chemopreventive agents that have the prospect of being administered to women of childbearing potential. These will be the standard segment 1, 2 and 3 studies as described in the "Guidelines for Reproduction Studies for Safety Evaluation of Drugs for Human Use," available from the contract specialist upon request. For efficiency, the male rats from the three month oral study may be used to initiate the male related reproductive toxicity studies.

Task 4--Perform chronic one year oral toxicity in rats and dogs. Clinical laboratory studies and gross and microscopic necropsy findings are to be included.

It is estimated that up to four master agreement orders per year will be issued pursuant to the awards of the master agreement contracts.

Suitable facilities and equipment appropriate to accomplish tasks should be available. Animal holding facilities for dogs must be provided with adequate environmental containment. Animal facilities must meet LTAALS specifications. Facilities must have design and maintenance capability to meet chemical and biological control; must comply with NCI carcinogens and handling standards; must comply with federal and state occupational health and environmental laws and regulations. On site data handling (computer), chemical, and pathological facilities and equipment should be available.

Contract Specialist: Alan Kraft
RCB Blair Bldg Rm 2A07
301-427-8745

RFP NCI-CN-75425

Title: Evaluation of chemopreventive agents by in vitro techniques

Deadline: Approximately May 15

The required services will be defined by master agreement orders issued during the one year period of performance. This is a reissuance of a master agreement announcement and is being reissued with the intention of seeking new sources and enlarging the current pool of master agreement holders.

Pursuant to the master agreement orders the contractor shall screen and evaluate the activity of chemopreventive agents in various in vitro assays of cell transformation. Agents with potential chemopreventive activity are identified by epidemiologic surveys, initial laboratory (experimental) findings, observations in the clinical setting, or structural homology with agents having known chemopreventive activity. A rigorous and systematic evaluation of these candidate agents is necessary before their efficacy can be examined in clinical trials for cancer prevention. In vitro screening and evaluation techniques measuring the ability of these chemopreventive agents to inhibit transformation provides a relatively rapid and efficient means of qualifying these agents for further evaluation for the prevention of cancer in humans.

Agents to be investigated by this project are potentially hazardous. The in vitro systems may involve the use of carcinogens, tumor cells or tumor viruses. Laboratory practices shall be employed which will keep any element of risk to personnel at an absolute minimum. Where indicated, tissue and compound handling must be performed in (at least) class 1 laminar flow cabinets which must meet NIH specifications for work with these agents. The offeror shall comply with NCI safety standards for research involving chemical carcinogens.

It shall be required that the facilities have operating tissue culture/cell biology and chemistry laboratories which are suitable for using hazardous and/or carcinogenic materials as test materials.

It is estimated that up to 10 task orders per year will be issued pursuant to the awards of the master agreement contracts.

The contractor must have or be able to obtain all the equipment necessary to accomplish the studies, including but not limited to, laminar flow hoods, CO_2 incubators, equipment for sterility testing, isotope counters, spectrophotometer, hazardous chemical storage cabinets and refrigerators, equipment such as microscopes and miscellaneous laboratory equipment. The laboratory shall have or have access to appropriate terminal and computer facilities and equipment for data collection and storage.

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RFP NCI-CP-EB-71081-56

Title: Support services for genetic factors in persons at high risk of cancer--genetic markers for linkage analysis

Deadline: Approximately April 7

The Clinical Epidemiology Branch and Environmental Epidemiology Branch of the Epidemiology & Biostatistics Program in the Div. of Cancer Etiology are seeking contractors to provide laboratory support for genetic linkage studies whose goal is to map genes causing cancer to specific chromosome regions. These studies will involve the analysis of familial segregation patterns of cancer or preneoplastic syndromes in conjuction with those of polymorphisms of protein (usually in erythrocytes and serum) and of DNA (i.e., RFLPs) with known chromosomal locations.

NCI staff will ascertain families in which living persons in at least three generations have a known or suspected autosomal dominant trait which causes or is associated with cancer. Blood and sera from both affected and unaffected members will be submitted to the contract laboratories to be assayed for at least 30 different protein polymorphisms distributed throughout the genome and for about 50 DNA polymorphisms which in total cover every chromosomal arm. Genetic linkage analyses of the assay results and pedigree data will be carried out by NCI staff to determine if the results provide evidence for the chromosomal localization of the conditions under study.

Because two different types of laboratory approaches are required for this project, the work is separated into two categories. Respondents can propose to do either or both categories of work.

Assay A: Assays of protein polymorphisms.

Assay B: Assays of DNA polymorphisms.

Assay A is a recompetition of an existing contract. It is anticipated that one or two incrementally funded, cost reimbursement, completion type contracts will be awarded for a five year period.

Contract Specialist: Donna Winters
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