THE CANCER LETTER INTERACTIVE

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New Treatment For CML Could Be Model For Molecular Target-Based Therapeutics

NCI and Novartis Pharmaceutics Corp., of East Hanover, NJ, plan to design a multicenter clinical trial of a promising new oral agent for chronic myelogenous leukemia, STI 571, Institute Director Richard Klausner said this week.

Since STI 571 is one of the first agents developed specifically to act on a molecular abnormality present in a human cancer, the study could serve as a model for future clinical testing in the emerging field of molecular target-based therapeutics, Klausner said at a Dec. 7 meeting of the National Cancer Advisory Board.

Most CML patients carry an abnormality called the Philadelphia

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In Brief:

Maryland Wins Center Planning Grant; CTRC Receives $5 Million To Endow Chair

UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE was awarded a cancer center grant from NCI for fiscal year 1999. The three-year, $790,000 award makes the School of Medicine one of only six medical institutions nationwide with active planning grants from NCI. It brings UMSM and its partner, Greenebaum Cancer Center, a step closer to becoming an NCI-designated Cancer center. **Sanford Sass** is the director of the Greenebaum Cancer Center and professor of pathology and medicine and director of the Program in Oncology, UMSM. . . . **CANCER THERAPY AND RESEARCH CENTER** was awarded $5 million to endow the director's chair of the CTRC Institute for Drug Development. Funded by the SBC Communications Inc. Foundation, the grant becomes part of the $15 million needed to endow a total of six chairs for the IDD. CTRC is involved in a $35 million capital campaign to support new clinical treatment space and expansion of its laboratory research facility. . . . **BUNTING BLAUSTEIN CANCER RESEARCH BUILDING,** the new $59 million Johns Hopkins Medical Institutions comprehensive cancer center and research facility was dedicated Dec. 6. The building, which will serve as a hub for researchers, is named for the Bunting family and the Jacob and Hilda Blaustein Foundation for their donations of $10 million each to the Building campaign. The State of Maryland, private donors, NCI, and Johns Hopkins Medical Institutions provided additional funding. NCI Director **Richard Klausner** delivered the keynote address. . . . **$11 MILLION IN HIV/AIDS CARE** will be awarded by the Health Resources and Services Administration

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STI 571 Results Herald New Era Of Molecular Therapeutics

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chromosome, that results from the exchange of chromosomes 9 and 22. The exchange produces a protein called bcr-abl, a member of a family of enzymes called tyrosine kinases. STI 571 inhibits the c-abl, bcr-abl, and platelet-derived growth factor receptor tyrosine kinases.

CML is diagnosed in about 5,000 people in the U.S. annually. Though there are a variety of therapies for CML, overall cure rates are only about 20 percent, Klausner said.

Results of a phase I study of STI-571 were presented at the American Society of Hematology meeting in New Orleans on Dec. 5, by Brian Druker of Oregon Health Sciences University in Portland. Collaborators included Moshe Talpaz, of M.D. Anderson Cancer Center, and Charles Sawyers, of the Jonsson Cancer Center at University of California, Los Angeles.

Patients were eligible if their disease tested positive for the Philadelphia chromosome, was in the chronic phase, and had failed interferon therapy. In the study, 54 patients completed at least four weeks of therapy at 10 dose levels ranging from 25 to 500 mg. All patients treated with doses of 140 mg or greater have had a hematologic response, defined as a greater than 50 percent decrease in white blood cell counts sustained for at least two weeks.

All 31 patients taking at least 300 mg a day of the agent have had complete hematologic responses, defined as normal white blood cell and platelet counts, maintained for at least four weeks.

Cytogenetic responses were achieved in 33 percent of patients treated with 300 mg or more within two months of initiating therapy. Two patients achieved a complete cytogenetic remission, confirmed by FISH analysis, at five months of therapy.

Side effects of therapy have been minimal and no dose limiting toxicities were encountered. At doses of 300 mg and higher, myelosuppression occurred in seven patients (five grade 2 and two grade 3).

"The potential significance of this type of research extends beyond leukemia," Druker said in a press statement released by OHSU. "One of the major goals of cancer research has been to identify differences between cancer cells and normal cells so that these differences can be targeted with more effective and less toxic treatments. That's exactly what we've seen happen in these patients."

The research was supported by NCI and the Leukemia Society of America.

Klausner said he met with Druker and officials from Novartis. NCI will expand the multicenter clinical trial to include several target assays that had not been tested, Klausner said. These assays are expected to provide further information about the new agent's activity.

Novartis has begun a phase II trial of STI 571 at 19 sites in the U.S. and Europe. Tests in children could begin early next year. Additional trials are planned for patients with advanced-stage CML, as well as Philadelphia chromosome positive acute lymphocytic leukemia, the company said.

"STI 571 has demonstrated some promising results at a very early stage, and Novartis recognizes the impact it may have on CML patients," Manny Litchman, leader of the STI 571 project at Novartis said in a press statement. "This phase II study will provide valuable information about the compound as we further accelerate its clinical development."

Further information on patient eligibility for the studies is available from Novartis at 800-340-6843 (in the U.S.) or from the company's website at http://www.novartisoncology.com. Patients and physicians outside the U.S. may contact the medical department of the local Novartis Pharma Co. or consult the "contact us" section of the company's website at http://www.pharma.novartis.com.

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Founded Dec. 21, 1973, by Jerry D. Boyd

Another study of STI 571 that Druker's team at OHSU presented at the ASH meeting demonstrated that the agent also selectively inhibits the tyrosine kinase activity of c-kit, another receptor. The agent therefore may be useful in treating cancers associated with increased c-kit activity, including mast cell malignancies, gastrointestinal stromal tumors, seminoma, acute myeloid leukemia, small cell lung cancer, and breast cancer.

Further information and abstracts are available on the ASH website at http://www.hematology.org.

Model for Molecular Target-based Trials

NCI has re-oriented its drug development programs to make molecular target-based drug discovery a high priority. Two new grant programs were established earlier this year to fund research to identify promising targets and develop new therapies to attack those targets (**The Cancer Letter**, July 2).

In its professional judgment budget, the Institute proposes spending $66.4 million in fiscal 2001 to identify and characterize targets, develop assays, establish chemical and biochemical diversity libraries, foster interactions between assays developers and diversity libraries, screen compound libraries, create tools and methods for target-based clinical testing, expedite preclinical development, expand distribution systems for biological resources and develop databases of drug screening results. The budget proposal is available at http://2001.cancer.gov/.

NCI's Rapid Access to Intervention Development program will receive new funding of $8.9 million this year for contracts for academic drug discovery needs, Klausner said.

Druker's preclinical and clinical studies "very nicely describe some aspects of molecular targets approach to drug development and testing," Klausner said to the NCAB.

Druker was looking for an agent that would specifically inhibit bcr-abl. Searching through compound libraries at Ciba-Geigy, which later became Novartis, Druker found STI-571.

"This agent does appear to represent an example of a promising drug," Klausner said. "We will now have to see what this drug alone really does long-term. Does it affect survival? Patients in blast crisis will respond, but this is not a sustained response.

"You have an agent designed to inhibit a kinase," Klausner said. "We want to know in a molecular target-based clinical trial, is the kinase in the leukemic cells of the patients being treated inhibited, and how completely, with what kinetics, and what persistence?

"What's impressive about this [study] for the issue of targets goes back to this phrase that Bob Wittes [director of the NCI Division of Cancer Treatment and Diagnosis] has gotten all of us to use, of 'credentialing' targets," Klausner said. "That is, the accumulation of the experimental evidence that says that a target associated with a cancer actually is mechanistically both causative of the development of the cancer, but more importantly, required in the cancer for its survival, growth, and behavior."

There are few molecular targets in cancer for which scientists have conducted these types of experiments, Klausner said. "This represents one of the best," he said.

"This translocation product is causative to the development of this leukemia," Klausner said. "We also know from a variety of studies that an active kinase is required. Most importantly, we know that if you take the leukemic cells and [conduct] a variety of experiments, that the continued activity of the kinase is required for the survival of the leukemic cell."

"With all of that, one can say with this fairly well-credentialed target that this kinase might be a good target specific for CML," Klausner said.

Clinical trials using molecular target-based therapies must test "not only what happens to the individual patient, but also the target," Klausner said. "If we are going to develop target-based therapies, we are going to need to know in the context of clinical trials, whether the targets we have so cleverly chosen are valid, whether the drug is affecting the target appropriately, and whether the expected cellular responses are actually happening. So we turn this whole system into one where we gain real evidence about the progress we are making, as opposed to a blinded system where we are only looking at outcomes."

Era Of Molecular Approaches To Cancer

In remarks last month at what was probably the largest scientific meeting held in the U.S. that was devoted specifically to molecular target-based therapies in cancer, Klausner said the era of molecular approaches to cancer is beginning.

"Though the changes seem to be happening quickly, it is going to remain a very difficult process," Klausner said. "We are likely going to be lucky in some cases, but the challenge of deeply understanding

what we mean by targets, how we relate an effect on a target with the outcome continues to be a very daunting problem."

"On the other hand, we are at what most of us think is a fairly transforming time in science, when at least the pieces of the puzzle, for the first time ever, all the pieces, can be laid out before us and actually looked at and hopefully, interpreted," Klausner said. "Where new technologies give us access to looking at the nature of cells and organisms and their biochemical and genetic complexity, they allow us to not only fulfill the productive era of reductionism, but actually finally move to synthetic approaches that will enable us not just to draw cartoons, not just argue about our favorite pathway and target, but actually step back and let the cell and the organism talk to us."

About 1,900 participants attended the meeting, "Molecular Targets and Cancer Therapeutics," held in Washington, DC, and organized by NCI, the American Association for Cancer Research, and the European Organization for Research and Treatment of Cancer.

NCI official Wittes said the meeting represented "a next step" in the evolution of cancer drug development. "If we are to really move our field in the manner that scientific opportunity allows now, what we are going to have to do is orient discovery, development, and clinical testing toward the mechanisms that we know are important in cancer biology and mechanisms that make the cancer phenotype what it is," Wittes said.

The process of drug discovery will have to "move towards science and to the extent possible, away from empiricism," Wittes said. "It doesn't mean that empiricism will play no role. It doesn't mean that serendipity will play no role. To the extent that we can, the object is to make a science out of what it is that we are doing."

However, clinical testing of target-based agents will be "a huge challenge," Wittes said. "How do we make the clinical end of this as mechanistically oriented as we can so that what we end up with is a validation in the clinic, not merely a test, not merely endpoints, but endpoints that actually validate the premises on which discovery is based? The object is to intensify this in the years ahead."

The three organizations have scheduled the next Molecular Targets meeting for Nov. 7-10, 2000, in Amsterdam. The meeting will be held in the U.S. and Europe in alternate years. Further information is available from AACR, phone 215-440-9300, email: meetings@aacr.org or on the AACR website at http://www.aacr.org.

NCI Programs:

Researchers Take "Director's Challenge" To Develop Molecular Profiles Of Tumors

NCI has awarded the first 10 grants of a new research program to define the patterns of molecular changes in tumors.

The program, titled "The Director's Challenge: Toward a Molecular Classification of Tumors," will attempt to discover molecular profiles that would have the potential to lay the foundation for the precise molecular diagnosis of cancer. Currently, cancers are diagnosed primarily based on the microscopic appearance of tumors and their clinical staging.

If successful, the new tumor classification schemes will more accurately reflect an individual patient's risk of the cancer progressing. "Correct and informative diagnosis is the cornerstone of modern medicine," NCI Director Richard Klausner said. "This initiative will begin the next great intellectual leap forward in accurately diagnosing cancer by defining, for the first time, the very molecules that are driving the growth of individual tumors."

As part of the initiative, investigators will work collaboratively, with the assistance of NCI staff, to identify ways to represent research data, so that other cancer researchers can interpret and analyze it. They also will develop strategies for publicly releasing research data. This approach to data sharing should significantly increase the value of the data, and maximize the NCI investment in molecular-based tumor classification research, NCI said.

The 10 five-year grants, totaling $4.1 million for the first six months of funding, were awarded to:

—Stanford University School of Medicine, Patrick Brown, principal investigator, $914,581, to develop molecular-based tumor classification schemes in breast and prostate cancer.

—University of Nebraska Medical Center, Wing Chan, $379,106, to develop molecular profiles in non-Hodgkin's lymphomas.

—Memorial Sloan-Kettering Cancer Center, William Gerald, $450,035, to develop molecular profiles that distinguish androgen-independent from androgen-dependent prostate cancer.

—Sidney Kimmel Cancer Center, San Diego,

John Gutheil, $537,736, to develop molecular-based classification schemes for organ-confined prostate cancer.

—University of Michigan Medical Center, Samir Hanash, $725,954, to develop molecular-based classification strategies in colon, ovarian, and lung cancers.

—University of Pennsylvania Center for Cancer Pharmacology, Philadelphia, Steven Johnson, $219,177, to develop molecular profiles in ovarian cancer.

—Dana-Farber Cancer Institute, David Livingston, principal investigator, to develop molecular-based classification schemes in early stage prostate and lung cancers.

—Fred Hutchinson Cancer Research Center, Jerry Radich, $193,189, to develop molecular profiles in several stages of chronic myeloid leukemia.

—The Wistar Institute, Louise Showe, $252,464, to develop molecular profiles that identify subgroups of cutaneous T-cell lymphoma.

—Medical College of Ohio, James Willey, $106,090, to develop profiles of chemosensitive and chemoresistant non-small cell lung cancer.

A second round of funding will take place later this fiscal year, following review of applications received last month, the Institute said.

Report Calls For Strengthening Of NCI Nutritional Research

NCI must strengthen the nutritional sciences research efforts in its Cancer Prevention Research Program, according to a report by an advisory group.

The report, "New Directions for Nutritional Research at the National Cancer Institute," looks at diet as a lifestyle choice that individuals are able to control when given the relevant information. "It is a logical focal point for cancer prevention strategies," according to the report, by the Nutrition Implementation Group. "Prevention must be the principal component of our nation's strategy to reduce the burden of cancer among Americans."

Based on a study by Doll and Peto (1981), which suggests that diet is a factor in one-third of all cancers, as well as other available evidence, the report makes clear "the existence of a clear link between nutrition and cancer is not in question." The challenge, said the report, is to define "the causal and mechanistic relationships between specific dietary constituents and cancers at various organ sites."

The implementation group, which includes 22 scientists from NCI, other federal agencies, and the extramural community, was charged with developing recommendations for the Cancer Prevention Research Program in two primary areas. First, develop ways for NCI "to encourage the broader involvement of the nutritional science community and simultaneously strengthen nutritional sciences to achieve more depth in the study of the nutrition-cancer relationships." Second, establish mechanisms by which molecular genetics and cell biology could be incorporated more fully into the study.

The report, presented to the NCI Board of Scientific Advisors last month, made the following seven recommendations:

1. Create a trans-NCI Coordinating Committee on Nutrition and Cancer led by the Division of Cancer Prevention.

2. Establish a number of programs of excellence in nutritional science and cancer prevention, including several at existing cancer centers. Allow an ample period to develop interdisciplinary Request for Application responses.

3. Provide developmental funds to encourage nutritional science-related pilot projects in existing cancer centers.

4. Hold interdisciplinary workshops linking basic areas of biology and nutritional sciences with cancer etiology and pathogenesis.

5. Enhance training and career development in the nutritional sciences aspects of cancer research.

6. Assure an appropriate mix of reviewers for diet and cancer research grant applications.

7. Invite nutritional scientists to join the NCI Board of Scientific Advisors.

The group's chairman was Vernon Young, professor of nutritional biochemistry, Massachusetts Institute of Technology. Other members were Bruce Ames, professor of biochemistry and molecular biology, University of California; Diane Birt, professor and chairman, Department of Food Science and Human Nutrition, Iowa State University; Timothy Byers, professor of preventive medicine and biometrics, Prevention Subcommittee on Nutrition and Cancer, University of Colorado; Johanna Dwyer, professor, Tufts School of Nutrition and Medicine and New England Medical Center; James Gaylor, professor of biochemistry, Emory University School of Medicine; Peter Greenwald, director, Division of Cancer Prevention, NCI; Edward Giovannucci, assistant professor of medicine, Harvard Medical

School; Vay Liang Go, associate director, University of California at Los Angeles Center for Human Nutrition; Samson Jacob, professor and chair , Department of Nutrition and Food Studies, New York University; Barbara Pence, professor of pathology, Texas Tech Health Sciences Center; Franklyn Prendergast, director, Mayo Cancer Center; Richard Rivlin, program director, Clinical Research Unit, Memorial Sloan-Kettering Cancer Center; Irwin Rosenberg, director, USDA Human Nutrition Research, Tufts University; Rachel Ballard-Barbash, chief, Applied Research Branch, Cancer Control Program, NCI; Carolyn Clifford, chief, Diet and Cancer Branch, Acting Associate Director, Cancer Prevention Research Program, Division of Cancer Prevention, NCI; Beth Yetley, director, Office of Special Nutritionals, Center for Food Safety and Applied Nutrition, FDA.

NCI Publishes New Atlas Of Cancer Mortality In The U.S.

NCI has published the Atlas of Cancer Mortality in the United States, 1950-94, showing the geographic patterns of cancer death rates in over 3,000 counties across the country over more than four decades.

The 254 color-coded maps in the atlas will make it easy for researchers and state health departments to identify places where high or low rates occur, and to uncover patterns of cancer that would escape notice if larger areas, such as states, were mapped, NCI said.

The atlas will not tell researchers why death rates are higher in certain localities than in others, but it will provide important clues for further in-depth studies into the causes and control of cancer, NCI said.

For the first time, the atlas includes maps for both white and black populations, since earlier mortality statistics lacked data that would permit a separation of blacks from the nonwhite category.

"It's not easy to sort out why cancer mortality rates vary among geographic areas and why they might be changing," said Joseph Fraumeni Jr., director of NCI's Division of Cancer Epidemiology and Genetics, and the senior author of the atlas. "It's natural to want to know why cancer rates are elevated in a particular area, but it's important not to jump to conclusions before careful studies can be conducted in these areas."

Many of the patterns displayed in the current atlas are similar to previous ones. High breast cancer rates have been seen for four decades in urban centers in the Northeast. Studies have shown that regional variations in breast cancer rates are partially, but not entirely, due to established risk factors, including late age at first birth, early menarche, and late menopause, and to certain other factors, including education and mammography history, NCI said.

Likewise, colon cancer mortality rates have been elevated in the Northeast for at least four decades. Dietary and nutritional factors are thought to be involved, but the specific causative elements are not clear, the Institute said.

The greatest changes have been with lung cancer, said Susan Devesa, lead author from NCI's Division of Cancer Epidemiology and Genetics. The national annual lung cancer rate among white men rose from 39 per 100,000 during 1950-69 to 69 per 100,000 during 1970-94. In earlier atlases, elevated rates were seen in men in the Northeast and Southern Coastal areas. The highest rates now occur among white men in broad stretches across the South, among white women in the far West, and among the black population in Northern urban areas, Devesa said. "These changes generally coincide with regional and time trends in cigarette smoking," she said.

The patterns of prostate cancer deaths, which in the past showed little distinct geographic variation, have also changed. High rates among white men are much more prominent now in the North Central areas. In contrast, among black men, rates are excessive in the Southeast, particularly in rural areas.

One study has already been initiated in response to the new atlas, NCI officials said. Bladder cancer among men has tended to cluster in the urban Northeast since the 1950s, particularly in areas with chemical industries. Previous studies in high-risk areas have also shown elevated risks among truck drivers and other workers exposed to motor exhausts. The main risk factor is cigarette smoking, which accounts for one-half of bladder cancer. But the new atlas has shown that Maine, Vermont, New Hampshire, and upstate New York have elevated rates in both sexes that have become more pronounced over time.

NCI is working with the states to study why this might be happening.

The Atlas of Cancer Mortality in the United States, 1950-94 is a continuation of the cancer mapping project in NCI's epidemiology program. The

first atlas with color-coded mortality maps at the county level was published in 1975 and covered the years 1950-69. The current atlas adds 25 years of data to the original atlas and compares the patterns for 1950-69 with those for 1970-94. In addition, for the first time, an interactive version of the data will be available on the Internet.

Web accessibility makes several new features possible. The maps, text, tables, and figures from the hard copy be downloaded from the Web site. Also, national and state mortality rates are available, as are the tabulated data used to generate the maps. The user can create customized maps on the Web site, for example, comparing rates in different time periods, for any cancer in any county. The atlas is available at http://www.nci.nih.gov/atlas.

Printed copies of the atlas may be ordered from the NCI Cancer Information Service at 800-4-CANCER (800-422-6237), or from online at http://publications.nci.nih.gov.

Funding Opportunities:
Program Announcements

PAR-00-013: Translation of Technologies to Detect Alterations in Human Tumors

The Technology Development Branch of the Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, NCI, invites Program Project grant applications proposing the application of comprehensive molecular analysis technologies to tumor specimens in order to address questions of importance in clinical cancer research. The PA provides a mechanism for supporting continued refinement and application of the technologies produced under other NCI technology development initiatives.

Recent advances in our understanding of cancer at the molecular level coupled with the on-going development of comprehensive molecular analysis technologies have great potential to change the way we diagnose and treat cancer patients.

Molecular analysis technologies have continued to develop rapidly since the initial release of this program announcement in Dec. 1996. The past three years have seen an explosion in the development of microarray technologies and many other technologies for the simultaneous detection of multiple molecular alterations in tissues. The technologies have largely been developed using model systems, and most have been developed solely for the research market or for marketing to large pharmaceutical companies. Cancer researchers have been increasingly interested in using comprehensive molecular analysis technologies to address clinical needs. The program announcement is designed to promote collaborations between clinical investigators and technology developers in the context of P01 grant applications.

The program announcement is primarily targeted to technologies that are ready for translation to the analysis of clinical tissue specimens. NCI is aware that molecular analysis technologies are at varying stages of development and that it is unclear which technologies will best serve clinical research.

The intention of NCI is to promote an integrated team approach, where technology developers and cancer researchers will work closely together to refine and adapt technologies to develop clinically useful systems. The technical challenges of these projects are expected to require input from a diverse group of investigators, such as engineers, pathologists, molecular biologists, chemists, biologists, and informatics specialists. The process of moving the technologies forward toward clinical application will require input from clinical cancer researchers with access to clinical specimens. The goal of the program projects should be the development of integrated systems that can analyze molecular alterations in large numbers of human clinical specimens.

The period of support for applications submitted in response to this PA may be for up to five years. This PA will be in effect for two years, up to and including the October 1, 2001 P01 receipt date.

Inquiries: Toby Friedberg, Referral Officer, Division of Extramural Activities, NCI, 6116 Executive Boulevard, Room 8062, MSC 8239, Rockville, MD 20852 (express service), Bethesda, MD 20892 - 8239, phone 301-496-3428; fax 301-402-0275; e-mail: tf12w@nih.gov

PA-00-018: Bioengineering Nanotechnology Initiative

Application Receipt Dates: Dec. 15, 1999; April 15, Aug. 15, and Dec. 15 in the years 2000, 2001, and 2002

The program announcement, issued as an initiative of the trans-NIH Bioengineering Consortium, invites grant applications for Small Business Innovation Research projects on nanotechnologies useful to biomedicine. Nanotechnology is defined as the creation of functional materials, devices and systems through control of matter at the scale of 1 to 100 nanometers, and the exploitation of novel properties and phenomena at the same scale. Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine. Moreover, nanotechnologies developed in the next several years may well form the foundation of significant commercial platforms.

The duration and amounts of individual grants awarded under this PA may be greater than those routinely allowed under the SBIR program. Few small businesses possess the highly specialized resources needed for nanoengineering. Therefore, the PA encourages team approaches to research in the belief that a synergistic

blend of expertise and resources may be needed to allow for stronger partnerships between the small businesses and other entities in phase I than can be developed with the funds usually available through this program.

Applications are encouraged from teams of investigators from commercial, academic and other sectors of the research community. Partners to the small businesses may play important roles in these projects and may receive appropriate support for their efforts. In addition to requiring collaboration from various sectors, it is expected that this initiative will require expertise from a variety of disciplines, including engineering, chemistry, physics, material science, engineering, and biology.

The Omnibus Solicitation for phase I SBIR grants is available at: http://grants.nih.gov/grants/funding/sbir1/SBIR.htm. For phase II, see the instructions at http://grants.nih.gov/grants/funding/sbir2/index.htm.

Inquiries: For NCI-related issues, Carol Dahl, NCI, Bldg. 31, Room 11A03, MSC 2590, Bethesda, MD 20892-2590, phone 301-496-1550; fax 301-496-7807; e-mail cd41x@nih.gov

PA-00-021: Senior Scientist Award

The Senior Scientist Award (K05) provides stability of support to outstanding scientists who have demonstrated a sustained, high level of productivity and whose expertise, research accomplishments, and contributions to the field have been and will continue to be critical to the mission of the particular NIH center or institute. The award provides salary support for award periods of up to five years as a means of enhancing the skills of the individual recipient and dedication to his/her area of research.

Inquiries: For NCI, Lester Gorelic, or Andrew Vargosko, Office of the Deputy Director for Extramural Sciences, Office of Centers, Training and Resources, Executive Plaza North, Room 520, MSC 7390, Bethesda, MD 20892-7390, phone 301-496-8580; fax 301-402-4472; e-mail: lg2h@nih.gov or av8b@nih.gov

NCI uses the K05 grant mechanism exclusively to provide stability of support for established investigators in cancer prevention, control, behavioral and population sciences to allow them protected time to devote to research and to act as mentors for young investigators. Investigators must be able to commit up to 50 percent effort to the program.

RFA Available

RFA AT-00-001: Centers for Complementary and Alternative Medicine Research

Letter of Intent Receipt Date: Jan. 7

Application Information Meeting: Jan. 21

Application Receipt Date: March 14

To promote high-quality research of CAM, National Center for Complementary and Alternative Medicine, NCI, and National Heart, Lung, and Blood Institute invite applications for Centers for CAM Research using the P50 Specialized Center grant mechanism.

The essential characteristics of a P50 Center include: (1) a strong, focused scientific program encompassing basic and clinical research that will have a clear impact on human disease and associated quality-of-life or disability issues; (2) a strong, innovative program to establish and monitor developmental and feasibility studies that can respond quickly to new research opportunities; (3) a strong career development program to develop and expand the scientific cadre of investigators dedicated to research on a specific disease entity or biomedical problem; (4) shared core facilities that increase the functional capacity of the Center; and (5) a willingness and commitment to work with other Centers and scientists in order to maximize research progress.

NIH anticipates making up to three awards with an estimated commitment from NCCAM of $4.5 million total costs to fund the initial year. NCI and NHLBI may provide support to other meritorious applications that fit their program objectives. Applicants may request three to five years of support. Applications submitted in response to this RFA are limited to $1.5 million total costs (direct costs and Facilities and Administration costs) in the first year of the award. Future increases are limited to three percent per year.

Inquiries: For NCI, Jeffrey White, Division of Clinical Sciences, NCI, NIH, 9000 Rockville Pike, ldg. 10, Room 3B38, Bethesda, MD 20892, phone 301-402-2912: fax 301-402-1001; e-mail jdwhite@helix.nih.gov

In Brief:

Slavkin To Leave NIH, Returns To USC; March Requests $10B

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for U.S.-Mexico border and migrant residents. Health and Human Services Secretary Donna Shalala , who made the announcement on World AIDS Day, said the grant will support four five-year demonstration projects and evaluation centers in Arizona, California, New Mexico and Texas. . . . **HAROLD SLAVKIN,** director of National Institute of Dental and Craniofacial Research at NIH, was named dean of the University of Southern California School of Dentistry. Slavkin had been on an extended leave of absence from USC during his tenure at NIH. . . . **CORRECTION:** In a Letter to the Editor in the Nov. 26 issue of **The Cancer Letter**, the amount targeted by The March Research Task Force for increasing the NCI budget over five years was incorrrectly stated. The Task Force has recommended a target of $10 billion.

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