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NCI Advisors Approve $50 Million Pilot For Human Cancer Genome Project

By Kirsten Boyd Goldberg

An NCI advisory board approved the institute's plan to spend $50 million over the next three years to test the feasibility of a large-scale project to identify genes involved in the development of the major cancers.

The NCI Board of Scientific Advisors voted unanimously Nov. 14 in support of the proposal for the first steps of the Human Cancer Genome Project.

The National Human Genome Research Institute will provide another $50 million to support high-throughput sequencing at its Medical Genome Sequencing Centers.

As outlined by NCI, the three-year pilot project would consist of the

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NCI Plans To Cut Access To The Cancer Letter; Insiders Allege Attempt At "Thought Control"

By Kirsten Boyd Goldberg

Top NCI officials said they intend to cancel the institute's subscription to The Cancer Letter and The Clinical Cancer Letter in what they described as "cost-saving measures."

In an internal memo dated Nov. 15 and addressed to the NCI Executive Committee, Dorothy Foellmer, special assistant to NCI Director Andrew von Eschenbach, wrote that "as part of the FY 2006 budget review process," the institute would eliminate site licenses to the two newsletters published by The Cancer Letter Inc., based in Washington, D.C., as well as Research Policy Alert, a daily news service published by F-D-C Reports, of Chevy Chase, Md., a unit of Elsevier.

The memo, a copy of which was obtained by The Cancer Letter, said the review process was initiated by NCI Chief Operating Officer John Niederhuber.

The Cancer Letter, a weekly, has been widely read at the institute for the past 31 years. Over the past four years, during the von Eschenbach era, regular readership grew to 600 subscribers, making it the most read publication at the institute's electronic library. According to NCI data, the number of subscribers at the institute grew by 180 over the past year alone.

Foellmer's memo said Niederhuber had reviewed "NCI's global or institutional subscriptions to non-scientific publications," and the three site licenses were "identified for termination."

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"No Plans To Spend $1 Billion" On HCGP, NCI's Barker Says

(Continued from page 1)

following components:

—Three or four Genome Characterization Centers, funded through cooperative agreements at $12 million per year, or a total of $36 million over three years.

—Five to seven Technology Development R21 grants funded at $1 million a year, plus $2 million a year from the small business set-aside funds, and $2 million a year from NHGRI.

—One biospecimen resource contract of $2 million per year to be funded from the NCI Office of Cancer Genomics and Biorepositories and Biospecimen Research.

—Bioinformatics core to be developed through the cancer Bioinformatics Grid, $3 million in year 2 for an RFA for innovation in data interrogation.

NCI has been planning the project for about two-and-a-half years, as it began to "wind down" the Cancer Genome Anatomy Project, said Anna Barker, NCI deputy director for advanced technologies and strategic partnerships. A subcommittee of the National Cancer Advisory Board formally proposed the HGCP earlier this year (The Cancer Letter, March 18, 2005).

The subcommittee, led by Eric Lander, director of the Broad Institute, and Leland Hartwell, president of the Fred Hutchinson Cancer Research Center, estimated the project would cost $1.35 billion over 10 years.

As the HCGP gained notice over the past several months, it has become a target of criticism in some scientific journals. Opponents have called it a "megaproject."

Over 10 years, the cost would be "a mere $12 billion at today's prices," George Gabor Miklos, of Secure Genetics, based in Sydney, Australia, wrote in the May 5 issue of Nature Biotechnology. The article's title was "The Human Cancer Genome Project—one more misstep in the war on cancer."

In a letter published in the Oct. 21 issue of Science, Stephen Elledge, a Harvard University geneticist, and Gregory Hannon, of Cold Spring Harbor Laboratory, argued that the project should be delayed "until advances in sequencing technology are achieved." The project's cost would be "the equivalent of 1,000 R01 grants," they wrote.

NCI: "No Plans" to Spend $1 Billion

In her presentation to the BSA, NCI's Barker defended the project. She said that she had originally been skeptical of the idea, but changed her mind. "I have become convinced that this will actually provide an absolutely enormous leap forward for this whole field," she said.

Barker said the concerns about cost were exaggerated. The pilot project's cost to NCI of $50 million "is the only number that's been batted around," she said.

"Outside the NCI, there has been a lot of conversation about a billion and a half dollars," Barker said. "We have no plans to spend a billion and a half dollars. There is no reason to think about spending a billion and a half dollars. This is not a set-up that the Cancer Institute has been lulled into some sense of complacency and we're just going to move into a large, billion-and-a-half-dollar project.

"We have actually undertaken something quite extraordinary," Barker continued. "We have, for the first time, really attempted in a very meaningful way to integrate what's going on in cancer with what's been going on in terms of sequencing the human genome. What we've tried to do is bring that expertise and that experience to cancer."

About $32 million of the cost will be recovered from scaling back funding of other projects that are nearing completion, including CGAP, the Mammalian Gene Collection, and HapMap, Barker said. "We will also pick up $3 million that we set aside to solve biospecimen problems," she said.

NHGRI Director Francis Collins, in a longer and more detailed talk, said the cancer genome project is

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

"probably near the very top of the list, if not at the top of the list, for promoting our understanding of what causes this terrible disease cancer and figuring out how we can do a better job of diagnosing, treating, preventing, and curing it."

The project "couldn't have been conceived of" three or four years ago, and represents a "unique, historic opportunity to discover the complete atlas of genetic alterations of cancer," Collins said to the board.

While researchers have found many genes involved in cancer, "we are still a little bit like the classic story of the guy who leaves the bar and realizes he has lost his keys and goes searching for them, but looks only where he can actually see" under streetlamps, while the keys are somewhere in the dark, Collins said. "We need to light up the streets here if we are really going to understand all of the mechanisms by which cancer comes about."

The proposal has been "widely misunderstood" as involving "mindless sequencing of lots and lots of DNA," Collins said. "There is gong to be lots of sequencing, because that will be a very exciting part of the project. But this is an integrated effort that will put together the sequence data with multiple other types of data," including copy number changes, gene expression patterns, epigenetic marks, DNA methylation, histone modifications, and transcription vector binding sites.

The cost "seems like a pretty good deal" for NCI, Collins said. "We propose to cover 50 percent of the cost. This is in spite of the fact that our budget is just about exactly 10 percent of that of the NCI.

"In fact, I've taken a lot of heat from the genome community on why did we agree to a plan of this sort where we are contributing the same dollar figure as NCI?" Collins said. "My answer to that is, we want to be full partners. We see this as an enormously exciting scientific opportunity…. It's the right thing to do."

The partnership will give the HCGP access to "the highest throughput sequencing facilities in the world," Collins said. NHGRI will soon recompete these facilities next year.

Collins pressed for approval of the pilot project without delay. "Our high-throughput sequencing facilities will expire from their current funding cycle in November 2006, so we need to put out an RFA to invite competition both from existing centers and any others that might be out there," he said. "We would like to include in that RFA explicit representation of the needs for cancer, and that's why the timing is pretty critical in terms of this meeting today, because we are going to go forward with this, and we would like to have that be a major part of what we are asking the sequencing centers to do.

"But we can't do this without the NCI," Collins continued. "If there is no Human Cancer Genome Project, our sequencing capacity will have to be applied to other problems, and in my view, that would be terrible waste of opportunity."

Board Seeks Info on Milestones, Specimens

A subcommittee of the BSA charged with evaluating the proposal recommended that NCI establish milestones that would determine whether to go ahead with the full-scale cancer genome project, said William Hait, director of The Cancer Institute of New Jersey and chairman of the subcommittee.

The subcommittee's level of support for the project "was very mixed, with some very enthusiastic… and some healthy skepticism" about the project's chances of success, Hait said.

"The main question is priorities," said board member Susan Horowitz, the Falkenstein Professor of Cancer Research at Albert Einstein College of Medicine. "There's no question we would get very interesting information and it would be very important, but also it's a very difficult financial time and we have to really seriously think about how to use our money."

Many of the scientific questions about the project "hopefully would be addressed in the pilot," she said.

"To me the major problem is how are we going to evaluate the pilot in three years?" Horowitz said. "Those of us who have been on the BSA a long time have seen that one of the most difficult problems is stopping something, because it becomes an institution unto itself."

Barker said the project would be "prioritized based on the availability of funds," after NCI sets the R01 payline. "We have made a real effort over the last year and a half to scale down genomics," in preparation for this project, she said.

"It's probably the most important thing that we could do in cancer with our money, period," Barker said.

Board member Richard Schilsky, associate dean for clinical research, University of Chicago, said he was "struck by the fact that there has been very little discussion in the documents that we are seeing at this meeting about the specimens, in terms of how the specimens would be selected, how they would be processes, how they would be stored, and even where the funding would come from—some funding would materialize in the Office of Biospecimens, but no

specific carve-out seems to be available to support the specimen acquisition and processing."

Barker said NCI had planned to put about $3.5 million into the biospecimen banking "for the past number of years," so the money has been set aside. NCI has identified "a few" biorepositories that have the appropriate collections for the pilot, she said.

The institute earlier this week issued a Request for Information from biospecimen repositories to find out whether existing collections could be used for the HCGP. Selection would be through peer review, Barker said.

Carolyn Compton, head of NCI's biospecimen office, said the project planners "came to a compromise position" on the type of tumor that would be used. "The choices are limited by technology, because we need a certain amount of tumor to extract enough DNA by the current technologies to go around to all the participants in this project," she said. "So that virtually eliminated these small, early-stage cancers. We need tumors that are bulky enough to have enough specimen."

Also, the project would look for cancers that by histologic phenotype have "as little heterogeneity as possible," she said. That would rule out metastatic tumors.

"We were very concerned with having these specimens be linked to uniform selection clinically and uniform treatment—therefore, appended to clinical trials with extensive annotation and follow-up data—if we are going to be able to interpret the biological and clinical significance of the findings," Compton said.

Barker said the pilot project would probably select one hematologic malignancy and one solid tumor.

"Why Call It A Pilot?"

Pressing NCI on the issue of outcomes, board member Mack Roach III, professor of radiation oncology at University of California, San Francisco, asked, "Why call it a pilot? Under what circumstances would you consider it a no-go? If it's a pilot, then let's be perfectly clear what the deliverables are."

Barker said the project will be evaluated on clinical relevance. "At the end of three years, we are going to [ask], what has come of out of the project in terms of better understanding process so that we can actually take better care of patients," she said. "Why do a pilot if we think it's so great? Because there are lots of technical issues here that we have to answer [before] we scale it up."

SCHILSKY: "It sure would be nice to have more discrete outcome measures. At the end of this pilot, we will not have a drug. We may possibly have a target for a drug, but we will not have a drug. You are highly unlikely to have a predictive marker for a drug, because that takes validation in a clinical trial. You might have a gene signature. So what, exactly, is one experimental outcome that, if you saw it, you would say, 'Ah ha!'"

BARKER: "The question you are raising is, what is that value added that we see that says we need to move quickly to scale this thing up? I think Francis made a point that we can't forget here. What we have created is an opportunity for dialogue. We have done something very extraordinary. We brought two cultures together. Our culture at the R01 level is doing a lot of what we are talking about here. But to bring that to a point where we can create a viable pipeline for sequencing, which is what we really need, and one that I think we can make work, what comes out of that? If we cannot, in this country, combine that very strong investigative base that we have developed with these advanced technologies to create value added for the American public in terms of new targets, new drugs, new diagnostics—then we've got a problem. So I think this cancer experiment, if that's what it is, is actually an experiment for all of biomedicine right now."

COLLINS: "I don't think you can expect this pilot, for three years, which represents 0.3 percent of the NCI budget, to answer every question in cancer. At the same time, I would be willing to put forward the notion that if this 0.3 percent doesn't generate, within three years, several new drug targets and several new diagnostic measures that enable us to stratify cancers that we currently lump together into a way that is clinically useful, then I would think this would have been a failure…. The reason we are doing this is to find out what is the potential here."

Board member Hait made a motion for approval of the pilot project with the following conditions:

—The full-scale HCGP wouldn't proceed unless the pilot project meets milestones listed on two slides that NCI staff presented.

—The proportion of funding for technology development grants for high-throughput cancer cell analysis would be increased from 7.5 percent of the total to about 15 percent of the total, to encourage more investigator-initiated research.

The milestones on NCI slides were as follows:

Key Success Factors of Assessing the Pilot Project

—Robust genomic analysis of two tumors that will identify thousands of genes/regions for re-sequencing.

—Clinically meaningful data.

—Analysis performed with sufficient power (>500

samples/tumor) to provide a "pipeline" for re-sequencing important (occur at >5-10% frequency) cancer genes/regions.

—Sequencing of ~30M sequence reads ~600 nucleotides each.

—Establishment of a public database of sequences, characterization of results, and clinical data that is widely used to support discovery and translational research.

What Is the Basis for a "Go/No Go" Decision?

—Ability to find and correlate genomic changes (e.g., copy number, deletions, amplifications) through in-depth gene sequencing.

—New cancer genes discovered from the tumors studied, not based on current understanding.

—Ability to differentiate tumor subtypes based on specific genomic alterations.

—Technology approaches are achieved that provide the ability to differentiate meaningful biologic data from "noise."

Lack of Specimen Information: "It's Just Weird"

Board member Jane Weeks, professor of medicine at Harvard Medical School and chief of population sciences at Dana-Farber Cancer Institute, said the proposal should include more information on the specimens to be used.

"I'm still totally confused about the specimen stuff," Weeks said. "I should point out that this is not the first time I've been totally confused. Over the last year that I've been here, for virtually every RFA that's come forward involving specimens, there has been inadequate specification of where they were going to come from, why it mattered, what the scientific rationale was.

"For the future, I would urge staff to work those issues out before the RFAs get to us, because the way this has been reconfigured, I'm terribly enthusiastic about the emphasis on shared specimens and standardization methods linked to discovery—I think that's a really positive change here," Weeks said. "But it's very dependent on what the specimens are, where they come from, how big they are, what kinds of patients—and all that is going to drive the science that comes out of it.

"It's disconcerting to me to hear that that will be figured out later, even whether the volume of specimens needed to achieve the vision laid out in the RFA exists in any place that's adequately consented and available now, is not clear to me," Weeks continued. "It's just weird that we are voting to set aside $50 million to work on specimens and we don't really know what they are or whether they exist."

Hait restated his motion to recommend that NCI clarify plans for selection and use of tissue. The board then voted unanimously in favor of the project.

Request for Information

NCI issued a Request for Information to solicit responses from investigators who have collected well-annotated cancer biospecimens.

"Any investigator with biospecimen collections within the United States or internationally is encouraged to respond to the RFI," the notice said. "The goal of this RFI is to identify and gather data about the characteristics of existing human tumor repositories. The information gathered from this process will help distinguish the key features of biospecimen collections that could meet the needs of the pilot cancer genome characterization project."

The full text of the RFI is available at http://grants.nih.gov/grants/guide/notice-files/NOT-CA-06-002.html. The closing date for responses is Jan. 12.

NCI Staff To Lose Access To Independent Coverage; Is It About Cost-Cutting?

(Continued from page 1)

Readers at NCI say they rely on The Cancer Letter for independent coverage of science news, including criteria for drug approval, conduct of clinical trials, and the gamut of issues that involve the politics and policy of science.

In recent years, coverage has included von Eschenbach's politicization of the institute and his pursuit of the optimistic goal to "eliminate the suffering and death due to cancer" by the year 2015. In recent weeks, The Cancer Letter has written about the conflicts of interest and commitment von Eschenbach faces in his dual role as acting FDA commissioner and NCI director.

This coverage, which was cited in many national publications, has led von Eschenbach to step down from his role as vice chairman of the board of C-Change, a coalition of cancer interests largely funded by the pharmaceutical industry and headed by former President George H.W. Bush.

The NCI's decision comes at a time when von Eschenbach faces growing scrutiny and opposition in Congress and advocacy groups.

"It's Radio Free Cancer," said one regular reader. "Our link to the outside world." The decision to cut the subscription is viewed as "thought control," institute insiders say. "NCI is reacting against coverage that doesn't follow the party line," said one.

Two years ago, NCI launched a weekly newsletter called the NCI Cancer Bulletin, that looks remarkably

similar to The Cancer Letter. The Bulletin is published by the government at its expense and is distributed free of charge. The official publication usually features inspirational articles by—and photos of—the institute's leaders.

Last year, NCI spokesman Nelvis Castro said the Bulletin's budget was over $500,000. It is unclear whether this figure includes the time NCI scientists and physicians spend on the publication. "The Bulletin people are constantly beating the bushes for happy news," said one official. "It sucks up time."

Altogether, the cancellations of site licenses would result in "an estimated savings of approximately $80,000," Foellmer wrote. "Such cost-saving measures, while modest, reflect well on NCI's stewardship of taxpayer dollars during this time of fiscal strain."

Of that amount, NCI paid The Cancer Letter Inc. $48,083 for the site license to the company's two publications in 2005. The license, which enables all NCI employees and contractors to read the newsletters, is scheduled to be renewed in mid-January.

NCI's budget for fiscal 2005 was more than $4.8 billion. The institute has 2,000 full-time employees and an equal number of part-time employees and fellows.

"Nothing could be more at odds with this Administration's stated procurement policies than to cancel the government's subscription contract for obtaining an extensively used and highly regarded private newsletter, while sinking much larger sums into an inefficient and inferior house organ," said Charles Tiefer, professor of government contracting at the University of Baltimore School of Law and former solicitor and deputy general counsel of the U.S. House of Representatives.

"Perhaps the Government Accountability Office could look at the highly dubious policy rationalizations being provided to explain why the Administration would replace its contract with the superior outside provider of science news with a much larger expenditure for a Pravda-like outlet," Tiefer said.

"I'm Counting On You To Make Me Look Good"

NCI officials in the Office of Communications approached The Cancer Letter in 2001 to discuss a site license. The fee was determined based on the number of individual subscriptions NCI employees were purchasing at the time. The license was put in place in 2002 and renewed every year since.

Justifying the institute's procurement in 2004, a notice in the Federal Register said the newsletter "represents a very timely, comprehensive information resource for NCI personnel."

An individual subscription to The Cancer Letter costs $335 per year. The Clinical Cancer Letter, a monthly newsletter covering clinical cancer research, costs $119 per year.

"You have the option to establish your own subscription agreement with these entities and pay for these subscriptions out of your operating budgets if you feel they are essential sources of information," Foellmer wrote in the memo to the Executive Committee. "Please contact [budget officials] John Hartinger or Lucy Greene if you have any concerns regarding this decision."

If all current readers at NCI purchase individual subscriptions, the institute will spend $201,000 on The Cancer Letter next year.

The day before Foellmer sent out her memo, NCI Chief Operating Officer Niederhuber approached this reporter during a break at the meeting of the NCI Board of Scientific Advisors. "I'm counting on you to make me look good," he said.

The Cancer Letter has covered NCI, other federal agencies, Congress, and cancer research in the U.S. since 1974.

The newsletter has won numerous awards for investigative journalism, including the 2004 Robert D.G. Lewis Watchdog Award from the Washington, D.C. chapter of the Society of Professional Journalists for coverage of von Eschenbach's NCI. The Cancer Letter is the only publication to have won this award three times.

The newsletter was a finalist for the 2003 Gerald Loeb Awards for Distinguished Business and Financial Journalism for breaking the story that led to the conviction of ImClone Systems Inc. founder Samuel Waksal for securities fraud.

Paul Goldberg contributed to this report.

In the Cancer Centers:

Vanderbilt Wins Renewal Of Meharry Partnership

VANDERBILT-INGRAM Cancer Center will receive renewed NCI funding to continue a partnership with Meharry Medical College. The U54 five-year renewal grant totaling $10 million will begin in April, when the current grant expires.

"We received a score of 147," where 100 is a perfect score, said **Harold Moses**, director emeritus of Vanderbilt-Ingram and co-principal investigator on the project.

"Over the last several years this funding has

allowed us to create the Clinical Trials Clinic at Meharry," said **Samuel Adunyah**, chairman of Biochemistry at Meharry and co-principal investigator on the grant. "We have 14 new faculty members, basic scientists, epidemiologists, three oncologists—we had none before."

To continue efforts to reach out to the African American community, Tennessee State University also is joining the collaboration, said Moses. **Baqar Husaini**, professor and director of the Center for Health Research at Tennessee State, said this marks the first time they have joined forces with a cancer center.

* * *

UNIVERSITY OF COLORADO Cancer Center received funding from a state tobacco tax to conduct the Colorado Tobacco Attitudes and Behaviors Survey. The study will examine smoking rates and attitudes about tobacco among state residents. From now through January, survey workers will call randomly selected homes to complete a 10-minute interview with 13,000 Coloradans. This is the second TABS survey to be conducted, considered one of the largest efforts of its kind.

"This second round will show us where we're making progress and where we need to work harder," said **Arnold Levinson**, head of the project.

Funding Opportunities:
Program Announcements

PAR-06-071: Dissemination and Implementation Research in Health. Letters of Intent Receipt Date: Dec. 26; Aug. 22; April 24, 2007, Dec. 26, 2008; Aug. 25; April 24, 2009. Application Receipt Date: Jan 24; Sept. 22/2006, May 24, 2007, Jan 24, 2008; Sept. 24; May 22, 2009

NIH invites grant applications to identify, develop, and refine methods, structures, and strategies that test models to disseminate and implement research-tested health behavior change interventions and evidence-based prevention, early detection, diagnostic, treatment, and quality of life improvement services into public health and clinical practice settings. The PAR will use the R03 funding mechanism. The PAR is available at http://grants.nih.gov/grants/guide/pa-files/PAR-06-071.html.

Inquiries: For NCI--Jon Kerner, 301-594-7294; kernerj@mail.nih.gov.

PAR-06-072: Dissemination and Implementation Research in Health. The PAR will use the R21 funding mechanism. The PAR is available at http://grants.nih.gov/grants/guide/pa-files/PAR-06-072.html.

PAR-06-067: Framework Programs for Global Health. Letters of Intent Receipt Date: Dec. 23. Application Receipt Date: Jan. 20.

Fogarty International Center invites applications for up to three years of support for multidisciplinary programs promoting global health research and teaching within and between institutions. NCI is interested in supporting global health through curriculum development and training efforts that focus on preventing and controlling the global use of tobacco. Training programs that consider the behavioral, socio-cultural, economic, and policy factors that help determine tobacco use are needed to equip scientists and practitioners with the appropriate knowledge and skills to effectively combat the tobacco epidemic. The award will use the R25 award mechanism. The PAR is available at http://grants.nih.gov/grants/guide/pa-files/PAR-06-067.html.

Inquiries: At FIC--Flora Katz, 301-402-9591; katzf@mail.nih.gov.

PAR-06-073: Small Grants for Behavioral Research in Cancer Control. Application Receipt Date: April 20; Aug. 21; Dec. 22; April 20, 2007; Aug. 22; Dec. 20; April 20, 2008; Aug. 21; Dec. 22.

The NCI program provides support for pilot or feasibility studies projects, development and testing of methodologies, development and testing of research technology, secondary analysis of existing data, self-contained research projects, or studies that provide a basis for more extended research. Examples of behavioral investigations in cancer control activities include the following areas: applied cancer screening; basic and biobehavioral research; applied research; health communication and informatics research; health disparities research; health promotion research; survivorship; surveillance research; and tobacco control research. The funding opportunity uses the R03 award mechanism The PAR is available at http://grants.nih.gov/grants/guide/pa-files/PAR-06-073.html.

Inquiries: Veronica Chollette, 301-435-2837; vc24a@nih.gov.

PA-06-064: **Basic And Preclinical Research On Complementary And Alternative Medicine**

National Center for Complementary and Alternative Medicine invites applications for funding of basic, mechanistic, and/or preclinical research in all domains of CAM, to understand mechanisms of action of CAM therapies and to provide a stronger foundation for ongoing and planned clinical studies. NCI is interested in basic, mechanistic, and preclinical research as it relates to the prevention, diagnosis and treatment of cancer as well as management of cancer symptoms and side effects due to conventional cancer treatment. Areas of interest include interactions between conventional cancer treatment and CAM modalities. The funding opportunity will use the R15 award mechanism The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-06-064.html.

Inquiries: For NCI--Wendy Smith, 301-435-7980; smithwe@mail.nih.gov. or Cindy Davis, 301-594-9692; davisci@mail.nih.gov.

NCCN National Comprehensive Cancer Network®

SAVE *the* DATE

NCCN 11th Annual Conference

March 8 – 12, 2006
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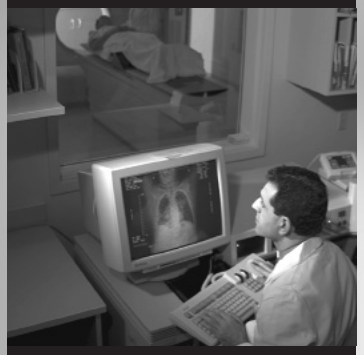
Hollywood, Florida



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SAVE THE DATE for the NCCN 11th Annual Conference featuring:

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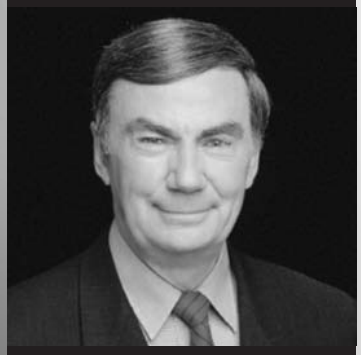

Roundtable Discussion:

Cancer Care in the 21st Century — Reality and Promise

Moderated by ABC News veteran and anchor Sam Donaldson

Register online at www.nccn.org

AC-N-0079-1105

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.

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