THE CANCER LETTER

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NCI Advisors Approve $144 Million Program For Nanotechnology Centers, R01 Grants

By Kirsten Boyd Goldberg

After hearing four scientific presentations from NCI grantees on the potential of nanotechnology as a platform for applications in cancer detection, imaging, and treatment, a panel of advisors this week approved the Institute's plan to spend up to $144.3 million on nanotechnology research over the next five years.

The NCI Board of Scientific Advisors July 12 unanimously approved the second version of the Institute's extramural research and training

(Continued to page 2)

In Brief:

CALGB Elects Schilsky To Third Term; House Panel Proposes 2.8% NIH Increase

RICHARD SCHILSKY was elected to a third consecutive five-year term as chairman of **Cancer and Leukemia Group B.** This was made possible by an amendment to the CALGB Constitution that changed the limitation on terms for the group chairman from two to three consecutive terms. In other changes at CALGB, **Everett Vokes** will succeed **Mark Green** as chairman of the Respiratory Committee. **Jeff Crawford** was appointed vice chairman. **Richard Goldberg** will succeed **Robert Mayer** as chairman of the Gastrointestinal Committee. **William Blackstock** was appointed vice chairman. **Leslie Kohman** will succeed **David Sugarbaker** as chairman of the Surgery Committee. . . . **HOUSE LABOR-HHS APPROPRIATIONS** subcommittee last week proposed increases for NIH and NCI of 2.8 percent above the current year's level. In its July 8 markup of the bill, the subcommittee matched the President's budget proposal, giving NIH $28.441 billion, an increase of $782.2 million from the current year's appropriation of $27.659 billion. NCI would receive $4.870 billion, the amount requested by the President, $130.8 million above the current year's appropriation of $4.739 billion. **Paul Kincade**, president of the Federation of American Societies for Experimental Biology, called the budget proposal "unprecedented, the lowest percentage increase that NIH has received in nearly two decades. Adjusting for the rising costs of research, it is a cut, with NIH estimating they will have to decrease the number of new and competing grants by 640. The erosion of our investment in NIH will decrease opportunities for scientists and discourage innovative, new investigators from entering the field. This will jeopardize our position as the world leader in health research. To rob the public of this hope, to cripple our progress in biomedical discovery, is both tragic and cruel."

NCI Cut $42 Million From Nano Program After BSA Criticism

(Continued from page 1)

program, two weeks after it tabled the original proposal for a $186.5 million program (**The Cancer Letter**, July 2).

"NCI has been terrifically responsive to the various questions and comments that we brought up," said BSA member Thomas Curran, chairman of developmental neurobiology at St. Jude Children's Research Hospital, who had criticized several aspects of the previous version. "I'm very enthusiastic about this revised [proposal]."

The centerpiece of the research initiative remains the same. NCI would fund three to five consortia, consisting of three or more institutions or programs that would form virtual "Centers for Cancer Nanotechnology Excellence." The centers would receive about $5 million a year each over five years, for a total of up to $90.8 million.

Under the revised plan, NCI would provide up to $38 million for 15 to 18 individual investigator-initiated R01 grants. The previous proposal alluded to the potential for R01 funding, but the new plan clearly specified a funding commitment for R01s.

Also, NCI removed two features of the plan that the board criticized at its June 24 meeting: a $7.5 million coordinating center and $6 million for cancer education grants. The second version of the proposal scaled back training grants from $50 million to $15 million. Altogether, as many as 30 fellowship awards would be funded under the program.

"This is the board at its best," said NCI Director Andrew von Eschenbach after the vote. "You have significantly helped us—forced us—to refine, define, and continue to improve. This is a much better proposal than we had envisioned at the outset of our previous meeting. It was your pointed, critical thinking, critical probing, questioning, and assessment that really helped to drive that maturation. We promise to continue to be open to that type of vigorous critique, because, in fact, it is really coming from the perspective of helping us to do the best for the cancer enterprise."

Four Nanotechnology Grantees

At the July 12 meeting, which was called specifically to address the nanotechnology concept, four NCI grantees presented their work in nanotechnology:

—James Heath, the Elizabeth W. Gilloon Professor of Chemistry at California Institute of Technology and a leader of the NanoSystems Biology Alliance, a collaboration between CalTech, the Institute for Systems Biology, and University of California, Los Angeles. Heath is a founding member of the scientific advisory board of Nanosys Inc., of Palo Alto, Calif., a founder and board member of Molecular Technologies Inc., and a board member of CTI Molecular Inc., of Knoxville, Tenn. He established and served as director of the California NanoSystems Institute, a research facility shared by UCLA and University of California, Santa Barbara.

—Arun Majumdar, professor of mechanical engineering at University of California, Berkeley, and a member of the Nanotechnology Advisory Group of the President's Council of Advisors on Science and Technology. In his research, Majumdar is collaborating with University of Southern California Norris Comprehensive Cancer Center and University of Pittsburgh Cancer Institute. He has begun discussions with FivePrime Therapeutics, of South San Francisco, to develop commercial applications of his work in biosensors.

—Rebekah Drezek, assistant professor of bioengineering, electrical, and computer engineering at Rice University. Drezek described work with nanoshells as platforms for cancer therapy, including a study of nanoshells to deliver thermal ablation to tumors in mice.

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—Sam Wickline, director of cardiology at Washington University, who holds two Unconventional Innovation Program awards from NCI. He founded Kereos Inc., of St. Louis, Mo., to develop commercial applications of his work, which involves targeted ligands and angiogenesis. The company has licensing agreements with Philips Medical Systems, Bristol-Myers Squibb Co., and Dow Chemical. Last year, Kereos, Dow, and Royal Philips Electronics became collaborators in a $2.8 million, three-year contract from NCI to Barnes Jewish Hospital and Washington University School of Medicine to create and evaluate contrast agents designed to seek specific molecular targets for potential cancer diagnosis.

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, introduced Health as "the sparkplug" for the NanoSystems Biology Alliance. "This is an individual who I believe is changing the world," Barker said. "His commitment to cancer is clear, and his commitment to get us to where we want to go is clear."

Heath, known for his work developing nanowires, advised NCI in formulating the nanotechnology proposal, sources said.

"Ann said I'm committed to this," Health said. "You can tell, because I'm wearing a suit. I didn't know I owned a suit." In his presentation, Health said nanotechnology would help NCI reach its "2015 goal" to eliminate suffering and death from cancer by providing techniques that would allow clinicians to detect disease early and monitor the response of patients to therapy.

Analyzing cancer cell lines and tissues, Heath's group is working to develop a model that would be able to stratify cancer by disease type and prognosis.

Right now, "these are large tools," Heath said. "What we would like to be able to do is reduce that to something that is trivially used that gives informative guidance to physicians. And I think more importantly, gives informative guidance to people who actually have the disease.

"I have this picture in my mind that is similar to how diabetic patients are able to monitor their insulin all the time," Heath said. "When they do that, they can modify their lifestyle and their diet in taking control of the disease.

"If you can monitor, in an informative way, the status of cancer in your body, I think, in a similar way, [you have] the opportunity to take control of the disease, not just for physician guidance, but for doing something else, sort of a biofeedback approach."

BSA member Enrico Mihich asked Health what he could do with the proposed NCI program that he couldn't do under existing grants. "You have made substantial progress already," said Mihich, director of sponsored programs at Roswell Park Cancer Institute.

HEATH: "There are many things we could do with it that we couldn't do without it. Let me give you a counterexample of the National Science Foundation and how they have directed their nanotech funds. The vast majority of nanotech funds in NSF has gone to investigator-initiated grants. I would argue that the amount of progress NSF has made in advancing the field is trivial, in spite of a huge investment. This technology has many uses, and there are two avenues we are pursuing, one is tuberculosis trials in South Africa, the other is cancer. I believe that cancer is overwhelmingly the best choice for this technology. I believe that once we get it to a certain stage, there is a way that it becomes commercialized, available to many people, that will never happen with TB.

"The databases that are being collected for cancer make this type of technology overwhelmingly best applied to cancer. What we can do without this technology, is we can develop a few toys and demonstrations, and we can look at two or three proteins. With it, we can develop full-fledged diagnostics."

MIHICH: "I think I was not clear in my question, because you are not answering it. We are not discussing the potential of the science. We are discussing the potential to implement the science in the absence of this program."

HEATH: "In the absence of this program, we will not have the opportunity to send the science out to cancer centers, we will not be able to make these platforms with enough throughput that researchers and clinicians in the cancer centers can use them. We can maybe take our two colleagues, Owen Witte and Charles Sawyers, and test it, but there is no way we can have the technology developed and vetted without a program like this. Is that a reasonable answer?"

MIHICH: "It is an answer."

Mauro Ferrari, a researcher at Ohio State University and an advisor to NCI on nanotechnology, said the four grantees exemplify the type of multidisciplinary scientists who would be supported

under the NCI nanotechnology program. "We can bring to the cancer world individuals and work that would be lost" without such a program, he said.

Now, NIH appears to have multiple nanotechnology initiatives. Ferrari developed a nanotechnology proposal for the National Heart, Lung, and Blood Institute. The NIH Roadmap also includes a nanotechnology initiative.

"NCI is taking the lead for the NIH trans-institute initiative in nanotechnololgy," von Eschenbach said. Nanotechnology "is going to be one of the most exciting things to happen for medical students in a long time," he said.

Nano-Oncology In "A Very Young Stage"

At the July 12 meeting, BSA member Curran said the board did its job in questioning the previous proposal. "As Andy [von Eschenbach] well knows, advisors are supposed to be outspoken and raise questions, and he is very fortunate that we are all outspoken people," Curran said. "The dialogue we go through in this iterative process is beneficial to all, and it has been educational for me. I'm really pleased and very happy with the way NCI responded.

"I think it's entirely appropriate that NCI plays a leadership role in the development of nanotechnology, and certainly the cancer field is at the forefront of needs for applications of this nanotechnology," Curran said. "The package that you put together—the combination of the centers, the training grants, and the platform technology support—I think is a very good one. It also leaves you with sufficient flexibility to respond to needs. It's a bit leaner and meaner, but that's not necessarily bad."

Some of the science funded by NCI "is truly innovative, that takes advantage of nanoscale properties," Curran said. "For the long term, that's where I see the true contribution of the nano world to cancer biology. However, I appreciate that it is long term, and so what you are looking at here is supporting not just a translation of available technologies to specific applications in cancer, but also the building of a ground base of support where this whole field can thrive, and truly innovative products will be developed."

The field may have difficulty with intellectual property and conflict of interest issues, Curran said. "I do encourage the NCI to play a role in trying to resolve some of these very complex issues," he said.

The nanotechnologists need to work with cancer biologists, Curran said. "One thing that struck me from the presentations is that the sophistication of the cancer biology is far behind the sophistication of the nanotechnology procedures at the current stage," he said. "That's understandable, because what you are doing is taking a very new scientific approach and applying it to this biological problem. But I do think the centers that you are establishing could provide you with a convenient interface to bring together top-level cancer biologists to help and inform decision-making as these technologies are being applied.

"It's not meant as criticism, just an observation that the field is in a very young stage, and as more cancer biologists come into the field and engage with engineers, I think you will see the sophistication level rise quite quickly," Curran said.

BSA Chairman Frederick Appelbaum, director of clinical research at Fred Hutchinson Cancer Research Center, said he was "particularly impressed" with the potential of nanotechnology for early diagnostics. "That's by far the most compelling for early translation," he said. "What Tom said about needing more cancer biologists is true, and also more clinicians. I think there is a certain naïveté about the clinical application that has to be addressed as this goes on. Forming these centers provides a very real mechanism for doing that.

"I'm enthusiastic overall about this, and I think there is going to be great potential," Appelbaum said.

Nonetheless, Appelbaum said he was concerned about establishing a long-term, large-scale program. "Every time we set up these large centers, they do a great job, and they probably are not going to go quietly into the night, and then this becomes a very hungry puppy that needs to be fed. Can anyone conceive of a way they would be ultimately integrated into cancer centers or SPOREs? Or is this going to become one more large mandate that is going to compete with the R01 pool?"

NCI program director Gregory Downing said NCI has developed performance milestones for the centers and "built-in mechanisms for sun-setting, based on reporting back to advisory committees."

"We hope that at the end of this, many of our cancer centers are engaged in nanotechnology platforms," Downing said. "My guess would be, much like many of our technology programs that we have come back to the BSA for more recently, that we would modify those to meet current needs."

"Our actions as a BSA can create entitlements that become self-perpetuating, and I'm worried about doing that around a technology that is not specifically

cancer-related," said BSA member Gilles McKenna, professor and chairman of radiation oncology at the Hospital of the University of Pennsylvania.

"Obviously, with funding getting tight, this program will be scrutinized intensively out in the community," said BSA member William Kaelin Jr., professor of medical oncology, Harvard Medical School. "I think the education process is just beginning.

"A number of us were part of an unplanned experiment in which we heard the nanotechnology presentation last night at the SPORE meeting, and heard this morning's presentation," Kaelin said. "The presentations this morning were much closer to what's needed. Last night, there was more jargon, more smoke and mirrors. There were assays and results being shown where the basis of the signals were not being explained. That only fed in, in my view, to a perception that maybe there is a little more hype here, and not so much substance. Today, I thought there were many more tangible results, and better distinction between what's a promise versus what's actually been produced."

BSA member John Minna said he was convinced that NCI should establish these centers. "I think this is another area where NCI can play a catalytic role, and not the least of which is to identify which are the really key clinical problems," said Minna, director of the Hamon Center for Therapeutic Oncology Research at University of Texas Southwestern Medical Center.

"[Former NCI Director Richard] Klausner and I had a big debate: He thought the big thing for arrays was to be able to identify where a carcinoma from an unknown primary rose from," Minna said. "Any oncologist will tell you it doesn't really matter, because there's nothing you can do about it. If you could identify what the treatment would be to cure it, it would. So you can go down a blind alley working on unimportant problems.

"The people who presented this morning were obviously very, very, incredibly smart and sophisticated people, and I can't tell you how important it is for you to understand that you are very naive about the clinical approaches that you have done," Minna said. "That's where I think the integration of cancer biology and clinical problems are important."

"I think NCI is key," Minna said. "In fact, in hearing the Andy and Anna presentation, it reminds me much earlier in my life about the Mork and Mindy TV show, because they talked about 'nano nano.'" [The ABC sitcom ran from 1978 to 1982, staring Robin Williams as an alien from the planet "Ork." He ended the show each week by saying "na no, na no," which meant "goodbye" in "Orkan."]

Excerpts from the concept statement follow:

The NCI Alliance for Nanotechnology in Cancer. Concepts for three new RFAs, first-year set-aside $16.2 million, total estimated $109.5 to $144.3 million over five years, three to five U54 awards, 12 R01s, 15 F32s, and 15 F33s. Program coordinator: Greg Downing.

Nanotechnology offers the unprecedented and paradigm-changing opportunity to study and interact with normal and cancer cells in real time, at the molecular and cellular scales, and during the earliest stages of the cancer process. Through the concerted development of nanoscale devices or devices with nanoscale materials and components, this initiative will bring enabling technologies for:

—Imaging agents and diagnostics that will allow clinicians to detect cancer in its earliest stages.

—Systems that will provide real-time assessments of therapeutic and surgical efficacy for accelerating clinical translation.

—Multifunctional, targeted devices capable of bypassing biological barriers to deliver multiple therapeutic agents directly to cancer cells and those tissues in the microenvironment that play a critical role in the growth and metastasis of cancer.

—Agents that can monitor predictive molecular changes and prevent precancerous cells from becoming malignant.

—Novel methods to manage the symptoms of cancer that adversely impact quality of life.

—Research tools that will enable rapid identification of new targets for clinical development and predict drug resistance.

Conceptual Framework: Based on the strategies outlined in the NCI Cancer Nanotechnology Plan, the Alliance for Nanotechnology in Cancer builds on the Institute's successes in building nanotechnologies and facilitates their integration into translational research. The Alliance supports the development of consortia of laboratories collectively identified as a "center" that consists of multidisciplinary teams of biological and physical scientists working together on specific projects that meet one of the six programmatic areas of emphasis. The centers will provide a nexus of interactions aimed at the assembly of components from materials sciences that will interface with biological systems that provide unique capabilities for conducting scientific explorations of the cancer cell at atomic level. Other components of the Alliance include individual investigator-initiated projects and career development initiatives to accelerate the translation of nanotechnology platforms in clinical

research. Collectively, these programs will facilitate the detailed examination and rigorous validation necessary to prepare promising agents and diagnostics for clinical trials.

Proposed mechanisms:

Centers for Cancer Nanotechnology Excellence: Cooperative agreement (U54). Each CCNE is a consortium of approximately four institutions or programs. Three to five CCNEs would be funded at $5 million each per year, for a total of $56 million to $90.8 million over five years.

The CCNEs are the core units of the science and technology programs supported by the Alliance. Each CCNE will function as a consortia or network of laboratories and research facilities organized to address one or more specific cancer nanotechnology platform needs. Each CCNE will be required to identify at least one of the following six programmatic areas of emphasis as its focus for technology platform development: molecular imaging/early detection, in vivo imaging, reporters of efficacy, multifunctional therapeutics, prevention and control, and research enablers. Within the context of the specific areas of emphasis identified, the CCNEs will offer the full range support necessary to develop products suitable for clinical trial assessment, from fabrication and synthesis of nanomaterials, to combinatorial assembly of components (vectors, targeting agents, and biosensors) to preclinical testing with animal models. It is expected that each CCNE will undertake to develop and prototype nanotechnology platforms, each with discrete milestones and a dedicated research team. Outcomes objectives (performance measures) for the CCNEs represent technologies that are developed and effectively utilized to overcome cancer processes.

Critical requirements for each CCNE include:

—Integration with a Comprehensive Cancer Center, SPORE program, or related NCI core programs.

—Affiliation with university or research centers of engineering and physical sciences (e.g., mathematics, chemistry, physics, and material sciences).

—Nanomaterials fabrication and synthesis capabilities.

—Facilities and expertise to support animal models and small animal imaging.

—Advanced biocomputing capabilities.

—Required existing not-for-profit/private technology development partnerships.

—Well-developed modules for integrative training in key areas relevant to the enterprise (e.g., biomaterials, clinical applications of nanotechnology).

—Education programs to disseminate information to the clinical oncology community.

—Technology assessment capabilities to identify and bring in new nanomaterials and nanotechnologies for cancer research.

Program management will be conducted through a steering committee with representation from each CCNE and NCI program managers.

Integration with existing resources: By balancing structured directives with investigator-initiated research, these centers will bring together the interdisciplinary teams and provide the infrastructure necessary to develop and translate nanotechnology advances to the clinic. Nanotechnology interfaces basic sciences, biomedical and clinical disciplines, engineering, and computer science, making coordinated program integration an essential component for the translation of discoveries into clinical application. CCNEs will therefore be required to provide training modules in relevant areas, such as biomaterials fabrication or clinical application of nanotechnology.

The CCNEs will be further integrated into a network of NCI resources that will assist to increase the visibility and availability of nanomaterials and nanoscale device technology within the cancer research and development communities. These include: Developmental Therapeutics Program; Academic Public-Private Partnership Program; Early Detection Research Network; Development of Clinical Imaging Drug Enhancers; Mouse Models of Human Cancers Consortium.

Through interactions with these NCI resources, as well as other federal and private sector groups, it is expected that this initiative will catalyze targeted discovery and development efforts and spawn new partnerships with the private sector. NCI will also implement established small business funding mechanisms, such as the Small Business Innovation Research and Small Business Technology Transfer programs, to interface with appropriate small business and R&D programs. As a result of this multi-faceted effort, new business development opportunities will be created and new frontiers of investigator-initiated research in the diagnosis and treatment of cancer will be launched.

Development of Multidisciplinary Research Teams through Career Development. Postdoctoral fellows, 15 F32 awards, and senior fellows, 15 F33 awards, total up to $15.5 million over three years.

Given the multidisciplinary nature of nanotechnology research, investigators with basic science and clinical backgrounds will require training to optimize the capabilities of the Alliance, particularly regarding the translation of nanotechnologies toward clinical oncology applications.

NCI will initially use existing training and career development mechanisms to direct talent to this area as quickly as possible and to incentivize cross-disciplinary research through training. When necessary, NCI will investigate innovative policy considerations, such as naming multiple principle investigators per project, as incentives for conducting team science. NCI will also encourage programs to be developed with interfaces to the training programs of other federal agencies as components of the National Nanotechnology Initiative. The advantages are to translate knowledge rapidly from fundamental nanotechnology sciences to directed

application in cancer biology.

Outcome objectives (performance measures) are represented by institutions with training programs and scientists and engineers who are trained in cancer nanotechnology. A three- to five-year benchmark is to support the entry of 20 to 30 scientists with formal training experiences in nanotechnology applied to cancer biology who can lead new programs in technology development through the new cancer research enterprise in the next five years and beyond.

Investigator-Initiated Research Projects. Bioengineering Grants and Partnerships (BRGs and BRPs, R01), total $38 million over five years.

Of key importance in the implementation of the Alliance for Nanotechnology in Cancer is the interaction of individual investigator-based projects with the centers. NCI has issued a Request for Information to identify opportunities, programs, and contracts for specified nanotechnology platforms in cancer research. From the input gained from the RFI process, NCI will develop concepts for individual Requests for Applications and Requests for Proposals that focus on technology development for specific nanotechnologies. It is anticipated that these research initiatives for developing and assessing nanotechnology platforms will be integrated with the Alliance initiatives presented here.

NCI anticipates using the R01 mechanism via Bioengineering Research Partnerships and Bioengineering Research Grants. The BRPs are designed to fund basic, applied, and translational multidisciplinary research that addresses important biological or medical research problems. In the context of this program, a partnership is a multidisciplinary research team that applies an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease, or to understand health and behavior. The partnership must include appropriate bioengineering or allied quantitative sciences in combination with biomedical and/or clinical components. The smaller BRG awards support multidisciplinary research performed in a single laboratory or by a small number of investigators that applies an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand health and behavior. A BRG application may propose hypothesis-driven, discovery-driven, developmental, or design-directed research at universities, national laboratories, medical schools, large or small businesses, or other public and private entities.

Program Assessment and Evaluation: NCI will track progress in six key areas: molecular imaging and early detection, in vivo imaging, reporters of efficacy, multifunctional therapeutics, prevention and control, and research enablers. During the first three years, NCI will accelerate selected projects that are already under way and catalyze the development of products that are primed for near-term clinical application. The following years will see projects come to fruition that reflect solving more difficult technological and biological problems or that require the integration of multiple technological components, but that have the potential to make paradigm-changing impacts on the detection, treatment, and prevention of cancer. Milestones reached during this latter period will also reflect the growth of the investigator pool that will be catalyzed by the Alliance.

Each RFA will include provisions for programmatic assessment that includes specific program milestones and outcomes objectives, as detailed in the Cancer Nanotechnology Plan.

Funding Opportunities:
RFAs Available

RFA-CA-05-010: Trandisciplinary Research on Energetics and Cancer

Letter of Intent Receipt Date: Oct. 15, 2004

Application Receipt Date: Nov. 16, 2004

NCI invites center grant applications, using the cooperative agreement U54 mechanism, to establish the TREC Centers in nutrition, energetics, energy balance, and physical activity. The centers will involve scientists from multiple disciplines and will encompass projects spanning the biology and genetics of behavioral, socio-cultural, and environmental influences on nutrition, physical activity, weight, energy balance, and energetics.

The centers will focus on two challenges in the area of energetics/energy balance and cancer: first, to enhance understanding of the mechanisms underlying the association between energy balance and carcinogenesis across the cancer continuum from causation and prevention through survival, and second, to develop effective innovative approaches with broad population impact at the social-environmental and policy levels for prevention of obesity with particular emphases on children and critical time periods during adulthood where weight gain is likely to occur, such as during smoking cessation, cancer treatment, and major life transitions involving work or family. The challenges require integration of diverse disciplines, spanning the full range of cancer research from the molecular biology of carcinogenesis to public policy research. The RFA is available at http://grants2.nih.gov/grants/guide/rfa-files/rfa-ca-05-010.html.

Inquiries: Linda Nebeling, chief, Health Promotion Research Branch, Division of Cancer Control and Population Sciences, phone 301-451-9530; fax 301-480-2087; e-mail nebelinl@mail.nih.gov.

RFA-CA-05-011: TREC Coordinating Center

Letter of Intent Receipt Date: Oct. 15, 2004

Application Receipt Date: Nov. 16, 2004

NCI Division of Cancer Control and Population Sciences invites applications for the U01 mechanism for

the establishment of a Transdisciplinary Research on Energetics and Cancer Coordination Center. The mission of the center is to promote collaborations among transdisciplinary teams of scientists, to facilitate data analyses, to examine common research questions across sites, to coordinate and facilitate semi-annual meetings of the TREC Centers, to develop training modules, and to evaluate progress. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-011.html.

Inquiries: See preceding RFA.

Pre-Application Conference Call for TREC Centers

TREC Concept Conference Call and Registration: Aug. 16, 2-4:30 p.m. ET. Information from the call will be posted to http://www.cancercontrol.cancer.gov/TREC.

Registration for the conference call is required. Register online at: www.scgcorp.com/trec-call2004.

Program Announcements

PA-04-125: Novel Approaches to Enhance Animal Stem Cell Research

The PA encourages the submission of applications for research to enhance animal stem cells as model biological systems. Approaches to isolate, characterize and identify totipotent and multipotent stem cells from nonhuman biomedical research animal models, as well as to generate reagents and techniques to characterize and separate those stem cells from other cell types is encouraged. Studies involving human subjects are not allowed under the PA. The PA will use the NIH R01 and R21 award mechanisms. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-04-125.html.

Inquiries: For NCI—Donald Blair, Cancer Cell Biology Branch, Division of Cancer Biology, phone 301-496-7028; fax 301-402-1037; e-mail blaird@mail.nih.gov.

PA-04-124: Studies of Energy Balance and Cancer in Humans

NCI invites investigator-initiated research applications to define factors affecting energy balance and to define mechanisms influencing cancer risk, prognosis, and quality of life. The studies may range from new analyses of existing datasets to additional collection of data and biological specimens in ongoing investigations. An applicant must have previously collected measures from human subjects on two or more of the following exposures: diet, physical activity, body composition, and/or related biomarkers (such as blood, urine, exfoliated cells, and/or tissue samples). Competitive supplements to existing NCI-funded grants as well as new R01s and R21s are invited. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-04-124.html.

Inquiries: Virginia Hartmuller, Epidemiology and Genetics Research Program Division of Cancer Control and Population Sciences, phone 301-594-3402; fax 301-402-4279; e-mail hartmulv@mail.nih.gov. Noreen Aziz, Office of Cancer Survivorship, phone 301-496-0598; fax 301-594-5070; e-mail na45f@nih.gov. Jackie Whitted, Nutritional Science Research Group, Division of Cancer Prevention, phone 301-496-0129; fax 301-480-3925; e-mail whittedj@mail.nih.gov.

PA-04-121: Understanding Mechanisms of Health Risk Behavior Change in Children and Adolescents

NCI, National Institute of Child Health and Human Development, National Heart, Lung, and Blood Institute, National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse, Office of Behavioral and Social Sciences Research, and Office of Dietary Supplements invite research grant applications that will enhance understanding of the factors and processes that influence the initiation, continuation, and/or cessation of one or more of the following health risk behaviors: substance abuse; inadequate exercise and poor dietary practices as they relate to being overweight or obese; and intentional and unintentional injuries. The PA will use the R01 and R21 award mechanisms. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-04-121.html.

Inquiries: For NCI—Louise Mâsse, Division of Cancer Control and Population Sciences, phone 301-435-3961; fax 301-480-2087; e-mail massel@mail.nih.gov.

RFP Available

RFP RFQ-NCI-40098-NV: Laboratory Services: Recombinant E-Selectin

Response Due Date: July 20

NCI on behalf of the National Institute of Neurological Disorders and Stroke, Clinical Investigation Section, Stroke Branch, Clinical Neuroscience Program Division of Intramural Research, is soliciting to attain clinical grade production of recombinant human E-selectin. This shall be achieved within clinical good manufacturing practice standards in sufficient volume for use in two clinical trials for two indications. The cloning and expressing is to be done in insect or CHO cells. Molecular mass specifications are open at the time. Recombinant E-selectin shall be purified and tested for safety, purity, identity, strength and potency. The contractor shall provide to FDA required documentation for human E-selectin in nasal spray formulation in three (3) dosages, in a timeframe allowing for production of the protein and submittal and approval of an IND application to FDA for start of clinical trials no later than March 2005. The RFP is available at http://www.fbodaily.com/archive/2004/07-July/08-Jul-2004/FBO-00615450.htm.

Inquiries: Deborah Moore, phone 301-402-4509; fax 301-402-4513, or Renita Smith, phone 301-496-8612, fax 301-480-0241; e-mail dm170b@nih.gov, s442i@nih.gov

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