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NIH Director Would Have Broad Authority Over Institute Budgets In Proposed Bill

By Kirsten Boyd Goldberg

The House Energy and Commerce Committee proposed legislation earlier this week that would give the NIH director vastly greater authority over the $28-billion budget of the agency, transforming the director's job from a relatively weak position managing a lose confederation of institutes into a powerful chief executive for setting biomedical research priorities.

Currently, Congressional appropriations committees establish the budgets of each of the 27 institutes and centers of NIH. The NIH director controls only the budget of his office, and can transfer 1 percent of the institute budgets into a fund for special initiatives.

Under the draft legislation released by the committee at a July 19 hearing, the NIH director would determine the budget for each institute. The director also could transfer an as-yet undetermined percentage, likely five or six percent, into a trans-NIH fund for "cross-cutting" research.

The proposal significantly alters the political debate over NCI's autonomy and "special authorities," which include Presidential appointment of the NCI director (The Cancer Letter, July 15). Cancer organizations have

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In Brief:

Senate Confirms Lester Crawford For FDA On 78-16 Vote After Criticism Of His Tenure

THE SENATE approved veterinarian and pharmacologist **Lester Crawford** as FDA commissioner July 18 on a 78-16 vote, despite criticism of his leadership as acting commissioner since March 2004. **President Bush** nominated Crawford to the position on Feb. 14, but the confirmation was held up by controversy, including allegations that Crawford promoted an employee with whom he was alleged to have had an affair. An investigation cleared him of that accusation. Also, **Sen. Patty Murray** (D-Wash.) and **Sen. Hillary Rodham Clinton** (D-N.Y.) vowed to block the full Senate vote until FDA ruled on the Barr Laboratories application for nonprescription sales of its emergency contraceptive Plan B. The Senators lifted their hold after **HHS Secretary Mike Leavitt** pledged that FDA would decide by Sept. 1. Murray and Clinton still voted against Crawford. Senators who endorse easier importation of Canadian prescription drugs also voted against Crawford. **Sen. Charles Grassley** (R-Iowa) criticized Crawford's tenure as characterized by a culture that silenced internal critics and shook the confidence of Americans through drug safety controversies **Sen. Edward**

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Legislation Would Remove Direct Appropriation To ICs

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urged the committee to maintain these authorities, which now appear relatively insignificant in comparison to losing direct appropriations from Congress.

The legislation would consolidate NIH appropriations into four line items: a division for the 15 "mission specific institutes," a division for the nine "science enabling institutes and centers," the Office of the Director, and a new Division of Program Coordination, Planning and Strategic Initiatives.

Committee Chairman Joe Barton (R-Tex.) said the bill is a "very high priority" for the committee. "We have doubled the agency's budget, but have not done anything to improve management," he said. Barton said he had strong bipartisan support for the legislation.

The committee expected to release a revised draft of the bill before the August recess. There is no companion legislation in the Senate as yet.

At the hearing, Republican members of the committee said NIH Director Elias Zerhouni can't do his job properly without the proposed changes.

"We must give the director the authority to manage the portfolio effectively," said Rep. Mike Ferguson (R-N.J.) "As Dr. Zerhouni said in the journal Health Affairs, 'If you have 27 fingers with no palm, you don't have a hand.'

"We need to do what we can to give you the upper hand," Ferguson said.

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However, several Democrats on the committee said they were uneasy about placing so much budget authority in one person.

"I think NIH works best when it's collaborative," said Rep. Anna Eshoo (D-Calif.). "I don't think it was ever meant to be an institute that has such a powerful director, so that there's only one conductor of the orchestra. I have concerns that … it will not improve Congressional oversight over appropriations."

Barton acknowledged that he had heard "a lot of concern" about the baseline funding for the institutes and centers. "My preference would be that the first year [after reauthorization], the baseline for each institute would be whatever it received in the current year," he said. "Then we would start from there and [the budgets] could go up or down. [After the first year], we would begin internal review and competition."

Zerhouni, the only witness at the hearing, said he favors that structure. "I believe the conceptual approach you have taken… is in my view a good approach," he said. "It's important that we don't disequilibrate [the institutes]. It would be very important to preserve the momentum."

In his testimony, Zerhouni spoke in favor of greater coordination that would allow NIH to quickly pursue new scientific opportunities. "I think the balance between the palm and the fingers is really our challenge," he said. "A strong palm with no good fingers is not a good hand. Strong fingers without a palm is not a good hand, either."

Congress and HHS would maintain its oversight role, and the NIH director's funding decisions would be the result of a collaborative, "transparent" process with intramural and extramural scientists, Zerhouni said.

"Excessive centralization is not productive in science, but do you want to have no coordination?" Zerhouni said. "The answer is no. The committee is proposing a structure that will accomplish this goal, which is parallel to what the [Institute of Medicine] recommendation has been, and parallel to what my own actions have been on the ground, when we try to develop trans-NIH programs such as the Roadmap for Biomedical Research."

The institutes and centers, known as ICs in NIH jargon, would remain focused on their individual missions, Zerhouni said.

"We need to make sure whatever we do doesn't supplant what has worked, or dictate IC-specific plans," he said. "I don't think we should go to the Cancer Institute and say, 'You shall do so.' I think it's more important that we stimulate explorations for part of

the portfolio of NIH to make sure that no stone gets unturned."

The legislation would transform NIH "from a structural organization to a more functional organization," Zerhouni said. "I do see a great wisdom is what the committee is proposing."

Budgets, Priority-Setting Main Concerns

The Federation of American Societies for Experimental Biology said it wasn't convinced of the wisdom of shifting total budget authority to the NIH director.

"Our 23 scientific societies remain concerned about the stated plan to eliminate the individual authorizations for each of the 27 NIH institutes and centers, and the provision to allow the NIH director to allocate and move money between the ICs," said Jon Retzlaff, director of legislative relations for FASEB.

"We believe the individual ICs must continue to have the authority to determine priority setting and strategic planning within their respective areas of scientific expertise," Retzlaff said. "We also hope the transfer authority will be clarified in the next draft, with specific percentages provided."

Two NCI advisory boards and the American Association for Cancer Research have said they were concerned about the preservation of "special authorities" granted to NCI in the National Cancer Act of 1971. These include Presidential appointments of the NCI director, the National Cancer Advisory Board and the President's Cancer Panel, as well as the mandate for NCI to submit a budget request, known as the "bypass budget," to the White House and Congress. NCI's bypass budget rarely has been matched by appropriations, but the document serves as a planning and communications tool.

The draft legislation appears to be silent on these authorities, presumably leaving them in place. NCI is the largest of the institutes, with a $4.8 billion budget for FY 2005.

Director Could Reorganize ICs

Under the draft legislation, none of the existing institutes or centers would be eliminated.

Currently, the HHS Secretary may reorganize NIH with notice to Congress. The bill would authorize the NIH director to reorganize the institutes and centers subject to the Secretary's approval, a public process carried out by regulations, and notice to Congress.

The bill also would allow the director, with HHS approval, to reorganize the Office of the Director. The director of an institute or center would be able to reorganize administrative units within an institute or center, with the NIH director's approval.

Other new authorities given to the NIH director would include program coordination, including conducting priority-setting reviews "to ensure that the research portfolio of the NIH is balanced and free of unnecessary, duplicative research," according to the committee's briefing paper on the legislation.

The director would be required to "assemble accurate data to be used to assess research priorities."

The director would be responsible for strategic planning and priority setting of "all research activities conducted or supported by NIH," and ensure that there are adequate resources to conduct projects identified in strategic plans.

Through the proposed Division of Program Coordination, Planning, and Strategic Initiatives, the director would identify research "important to the advancement of biomedical science" that involves more than one institute or center. The director would be able to award grants and contracts to support trans-NIH research, subject to approval by the Advisory Council of the Director. The research would have to go through peer review.

The division also would house various offices, including the Office of AIDS Research, the Office of Research on Women's Health, the Office for Behavioral and Social Sciences Research, the Office of Disease Prevention, the Office of Dietary Supplements, and the Office of Rare Diseases.

Under the bill, NIH would establish an electronic reporting system to list NIH research activities in a standard format.

The bill also would allow the NIH director, in consultation with the National Science Foundation and the Secretary of Energy, to award grants for demonstration projects "for research at the interface between the biological sciences and the physical, chemical, mathematical, and computational sciences."

Senate Appropriators Endorse NCI's "Bold Goal" For 2015

By Kirsten Boyd Goldberg

The Senate Appropriations Committee, in its report attached to the Labor-HHS appropriations bill, endorsed NCI Director Andrew von Eschenbach's goal to "eliminate suffering and death due to cancer by 2015" and asked him to outline how the goal could be achieved five years earlier.

"The committee applauds the director of the National Cancer Institute for setting a bold goal to

eliminate suffering and death due to cancer by 2015," the report said. "To assist Congress in establishing priorities, the Committee requests the Director to report to the Committee, by June 1, 2006, an outline of the progress made since the war on cancer was declared in 1971 and detail the specific steps that must be taken to achieve this goal by 2010."

At a hearing this spring, von Eschenbach said that with additional appropriations of $600 million a year, suffering and death from cancer could be ended by 2010. The statement was in response to questions from Sen. Arlen Specter (R-Penn.) (The Cancer Letter, May 20).

Three weeks ago, the House Appropriations Committee also endorsed the 2015 goal in its report (The Cancer Letter, July 1).

In the report's section on NIH, the committee said it "included sufficient funding to enable NIH to fully pay the committed levels on its grants," and will permit the average cost of new and competing research project grants to increase by 3.2 percent, rather than being held flat as proposed in the budget request.

The committee also criticized the Bush Administration policy on human embryonic stem cell research as "so narrow that it is stifling the pace of stem cell research." The committee said that with "proper safeguards," the research should be widened. "The committee strongly urges the Administration to modify the current embryonic stem cell policy so that it provides this area of research the greatest opportunity to lead to the treatments and cures for which we are all hoping," the report said. It also urged NIH to commit "a substantial amount of resources to all methods of human embryonic stem cell research."

The text of the NCI section of the Senate report follows.

National Cancer Institute—The committee recommends an appropriation of $4,960,828,000 for the National Cancer Institute. The budget request was $4,841,774,000. The fiscal year 2005 appropriation was $4,825,259,000. The comparable amounts for the budget estimate include funds to be transferred from the Office of AIDS Research.

Mission—The NCI conducts and supports basic and applied cancer research in prevention, early detection, diagnosis, treatment, and rehabilitation. The Institute provides training support for research scientists, clinicians, and educators, and maintains a national network of cancer centers, clinical cooperative groups, community clinical oncology programs, cancer prevention and control initiatives, and outreach programs to rapidly translate basic research findings into clinical practice.

Blood Cancers—The committee acknowledges some notable advances in the treatment of blood cancers, including leukemia, lymphoma, and multiple myeloma. These include several new drugs that have been approved and introduced to the market in the last 3 years, products of a strong public-private partnership. Despite new treatments, these cancers represent a serious health crisis. Almost 115,000 Americans will be diagnosed with these cancers in 2005, and nearly 55,000 will die from them. Moreover, the 5-year survival rates for these cancers lag behind the 64 percent 5-year survival rate for all cancers; the rate for multiple myeloma is only 32 percent, and for non-Hodgkin's lymphoma it stands at 59 percent. The committee encourages the Institute to strengthen its support for translational and clinical blood cancer research. The blood cancers strike individuals of all ages, races, and each gender, and serve as valuable prototypes for the development of therapies for all types of malignant disorders. The committee urges the institute to explore all mechanisms to support blood cancer research to improve treatment options and rapidly move discoveries from the laboratory bench to the patient's bedside.

Bone Marrow Failure Diseases—The committee encourages NCI to expand its research efforts into bone marrow failure diseases, including aplastic anemia, myelodysplastic disorders, and paroxysmal nocturnal hemoglobinuria. Each year, between 20,000 and 30,000 Americans are diagnosed with these diseases. In some cases, MDS, the most prevalent of these diseases, can progress over time to become acute leukemia. More research is critically needed to understand the causes of these diseases, develop effective treatments and cures, and prevent the progression of certain cases into leukemia. Furthermore, cancer patients who undergo chemotherapy often develop bone marrow failure diseases. The committee encourages NCI to gain a better understanding of the link between chemotherapy and these diseases, and to explore the development of alternatives means of treating cancer without causing the subsequent development of bone marrow failure diseases.

Brain Tumors—The committee believes that increased attention should be given by NCI and NINDS to brain tumor research. The committee encourages NCI to fund at least five Specialized Programs of Research Excellence in Brain Tumors grants in the upcoming fiscal year, with particular emphasis on those proposals which include both basic research and clinical treatment applications.

Breast Cancer—Breast cancer's toll continues to threaten the lives and the quality of life of thousands of women across all walks of life. In addition to ongoing research activities underway at the National Cancer Institute, the committee strongly urges the NCI to give increased attention to areas of research that focus on helping women to more fully restore and improve their quality of life after treatment, including further breast cancer research on lymphadema, stress, nutrition, exercise, weight, and the environment.

The committee remains concerned about missed opportunities in breast cancer screening, detection, prevention, control, and early diagnosis including those in mammogram detection, reading and analysis. The committee strongly urges the NCI to further accelerate advances in breast cancer screening technology and to capitalize on existing and create new technologies that improve early diagnosis, health outcomes, and survival.

Cancer Biobank—The committee believes that the cancer biobank, because it will centralize and standardize molecular annotation of tissues, has the potential to greatly accelerate the understanding of cancer and the discovery and development of new biomarkers, new diagnostics and new therapeutic approaches. Once established, the committee believes that it will be most efficient to utilize existing technologies such as high-density microarrays, given the long time frame for the development of new technologies.

Cancer Centers and Minorities—The committee commends NCI on the success of its cancer centers program. Given that minority populations suffer disproportionately from virtually every form of cancer, the committee encourages NCI to provide continued support for comprehensive cancer centers at minority institutions focused on research, treatment, and prevention of cancer in African American, Native Hawaiian, and other minority communities.

Cancer Metastasis—The NCI is encouraged to develop an interdisciplinary and integrated approach to study bone metastasis, by combining the expertise of oncologists, bone biologists and metastasis experts. Key issues to address include the generation of novel organ-like or mouse models which closely mimic tumor bone interactions that will pave the way for delineating novel mechanisms of how tumor cells go to the bone; the development of novel targets for better prognosis; and effective therapeutic targeting. Designing new strategies to make the bone microenvironment hostile to invading tumor cells is of high clinical relevance. The committee also urges NCI to expand research on osteosarcoma to improve survival and quality of life and to prevent metastatic osteosarcoma in children and teenagers who develop this cancer.

Chronic Lymphocytic Leukemia—This incurable disease is the most common form of adult leukemia in the United States. The committee once again urges the NCI to increase research into CLL, including improved therapies and their rapid movement from the laboratory to the bedside. The committee strongly urges the NCI to give favorable consideration to continuing and expanding the scope of research activities funded through the CLL Research Consortium as it works to defeat this devastating blood disorder.

Complementary and Alternative Cancer Therapies—The committee expects NCI to continue and expand its collaborative efforts with NCCAM to support research on promising complementary and alternative cancer therapies as well as on their integration with traditional therapies.

DES—The committee continues to support increased efforts to study and educate the public and health professionals about the impact of exposure to the synthetic hormone diethylstilbestrol. The committee expects NCI to continue to consult with organizations representing individuals impacted by DES as it carries out DES research and education efforts.

Gynecologic Cancers—In the last 5 years, approximately 130,000 women in the United States have lost their lives to gynecologic cancer. The committee commends the NCI for creating a cervical cancer and endometrial cancer SPORE, bringing the total number of gynecologic cancers SPORES to six, and expects that the NCI will expand the number of centers in the future. Unfortunately, 70 percent of ovarian cancer patients continue to be diagnosed in advanced stages when 5-year survival rates remain less then 25 percent. The committee encourages continued research by the four ovarian SPORES that will lead to a better understanding of prevention and the development of a screening tool offering women earlier diagnosis when this cancer is more curable. The committee also supports the expansion of NCI's collaboration with the NICHD for faculty development of gynecologic oncologists.

Health Cognition—The committee encourages NCI's Division of Cancer Control and Population Sciences to continue to build innovative collaborations such as the Health Cognition Group. The activities of this group of researchers are designed to plumb knowledge from basic research on how people process and use health information and synthesize it with the development and evaluation of theory-based

interventions to promote healthy behavior. Although these efforts are directed primarily to behaviors relevant to cancer, they will also serve the broader goal of developing theoretical frameworks that can be applied across a range of behavioral domains and conditions.

Health Communication—The committee acknowledges NCI's Division of Cancer Control and Population Sciences for developing HINTS, the first-ever survey to collect nationally representative information on the American public's need for, access to, and use of cancer information. Such a database is useful to practicing physicians, public health departments and policymakers, among others. HINTS provides an invaluable snapshot of how adults use the many information resources around them to lead healthier lives and to reduce the burden of cancer in America.

Hemophilia Cohort Study—The committee understands that NCI has made plans to discontinue research funding support of the Multi-Center Hemophilia Cohort Study. This cohort offers a database for improving the understanding of HCV and has served as the basis of significant peer-reviewed findings. The committee strongly urges the NCI to take all necessary steps to ensure the samples obtained through this cohort are preserved and accessible for future research. The committee also requests a report by May 1, 2006 on possible future research opportunities using the cohort samples.

Imaging Systems Technologies—The committee is encouraged by progress made by the NCI following its August 1999 conference on biomedical imaging, and it urges the NCI to continue to take a leadership role with the Centers for Medicare and Medicaid Services and the Food and Drug Administration to avoid duplicative reviews of new imaging technologies which may prevent their benefits from reaching patients on a timely basis. The committee is aware of the great potential for improved patient care and disease management represented by molecular imaging technologies, especially positron emission tomography through its ability to image the biology of many kinds of cancer and other diseases. The committee continues to support the NCI's increased emphasis on examining the molecular basis of disease through imaging technologies such as PET and MicroPET. The committee also continues to encourage the large-scale testing of women for breast cancer and men for prostate cancer to demonstrate and quantify the increased diagnostic and staging capabilities of PET relative to conventional diagnostic and staging technologies, including mammography.

Liver Cancer—The committee remains concerned with the increasing incidence of primary liver cancer, which is in sharp contrast to many other forms of cancer where the incidence is declining and the treatment options are rapidly increasing. The committee is aware that NCI, working with NIDDK, has convened an Experts Conference and is moving ahead with plans to increase resources dedicated to this disease. The committee urges NCI to make a substantial commitment to research on primary liver cancer with particular focus on the development of drugs that target the cancer without killing healthy cells by interfering with the cellular pathways of the disease. The committee further urges NCI to continue to support the NIDDK sponsored HALT-C clinical trial which has particular relevance to the NCI mission.

Lung Cancer—Lung cancer remains a major public health issue and is the leading cause of cancer death among women and minority populations. The death rate is expected to escalate as the population ages. The committee is encouraged by the success of new targeted drug therapies demonstrated in recent clinical trials in stage 4 patients. The committee encourages the NCI to work with the thoracic surgical community to initiate new clinical trials that involve patients at an early stage of the disease when surgery is a treatment option. The trials should test the effectiveness of these new drugs as adjuvant therapy to improve the outcome of established thoracic surgical therapy for lung cancer.

Lymphoma—The committee strongly urges that the NCI take bold action to address lymphoma as a public health problem and to capitalize on important research advances to date. While new treatments have become available for patients, more and improved treatment options are needed. The committee strongly encourages the NCI to boost its investment in translational and clinical lymphoma research. The committee commends the NCI and the NIEHS for convening a workshop on the viral and environmental links to lymphoma and recommends that steps be taken to strengthen the NCI investment in this area. The committee encourages the NCI to direct resources to: (1) studies of adequate scope to assure the identification of environmental risk factors for specific subtypes of lymphoma; (2) small studies designed to improve detection and quantification of historically difficult-to-measure environmental factors; (3) studies that are directed toward enhancing the understanding of the role of the immune system in the initiation and progression of lymphoma; and (4) studies that examine the simultaneous presence of a wide profile of infectious agents among individuals with lymphoma. The committee also encourages that resources be used

for research related to long-term survivors of both non-Hodgkin's lymphoma and Hodgkin's lymphoma. The committee strongly supports the recommendation of the Leukemia, Lymphoma, and Myeloma Progress Review Group [LLM PRG] that resources be invested in identifying the populations of patients that are at high risk of adverse outcomes from their treatment for lymphoma.

Mesothelioma Research—The committee is concerned with the pace of mesothelimoma research. This aggressive disease invades the lining of the lungs, heart, or stomach resulting in death in 4 to 14 months. To address these concerns, the committee strongly encourages the NCI to establish up to 10 mesothelioma centers, increase research, including clinical trials, detection and prevention methods, palliation of disease symptoms and pain management. The committee requests that the NCI issue a report, by June 1, 2006 on steps taken to address mesothelioma research.

Multidisciplinary Research—The NCI is commended for its innovative support of multidisciplinary training programs to enhance the scientific workforce. The committee encourages NCI to explore new opportunities with the Office of Behavioral and Social Sciences Research to increase the number of scientists who can bridge the realms of behavioral and social science research and public health or biomedical research.

Nanosystems Biology—The committee encourages NCI and the Office of the NIH Director to support a collaborative effort to bring nanotechnology, systems biology and molecular imaging together to examine the molecular basis of cancer. Initial efforts have shown that cancers such as breast cancer are not a single disease, but may encompass many different diseases, when examined at the molecular level. Many clinical trials of new drugs are now considered to fail if only 10 percent of patients benefit, yet the 10 percent may represent a specific type of the disease, where the drug may be 100 percent effective. Bringing these three disciplines together may allow researchers to identify specific sub-types of cancer and to better target new interventions. Successful results of such an effort could lead to a molecular classification of many types of cancer and to targeted molecular treatments for molecular-specific diseases.

Native Hawaiians—The committee remains concerned about the high incidence of breast, colon, and lung cancer among the Native Hawaiian population. The committee commends the NCI for its progress toward understanding and addressing the needs of the Hawaiian and Pacific Basin populations through its cooperative agreement with Papa Ola Lokahi and looks forward to a report of the prioritized health needs identified by those assessments.

Neurofibromatosis—The committee commends NCI for conducting clinical trials of NF1 patients. The committee is concerned about recent large drops in funding for NF research, and recognizing NF's connection to many of the most common forms of human cancer, the committee encourages NCI to substantially increase its NF research portfolio in such areas as further development of animal models, natural history studies, therapeutic experimentation, and clinical trials. The committee recognizes that basic research has successfully brought NF into the clinical era and encourages NCI to create, fund, and implement NF clinical trials infrastructures including NF centers, patient data bases, and tissue banks. The committee further encourages NCI to apply existing cancer drugs to NF patients in clinical trials both extramurally and intramurally, and to develop new drugs for NF which could then apply to the general population because of NF's connection to most forms of human cancer. The committee is aware of significant new advances in NF research in the past few years in the area of tumor suppression, and encourages NCI to continue to coordinate its efforts with other NIH institutes and government agencies.

Ovarian Cancer—Congress remains concerned that mortality rates associated with ovarian cancer have not seen the decreases that other cancer sites have experienced in the past 5 years. As the deadliest of all gynecologic cancers, ovarian cancer takes the lives of three-quarters of all women diagnosed with it within 5 years. Congress commends the National Cancer Institute for its recognition of the importance of studying this deadly women's disease and appreciates the NCI's recent investment that is helping to increase the understanding of the unique molecular pathways associated with ovarian cancer through its Specialized Programs of Research Excellence program. As such, Congress strongly encourages NCI to sustain and strengthen its commitment to and investment in ovarian cancer and maintain the SPOREs initiatives directed toward ovarian cancer in fiscal year 2006.

Pancreatic Cancer—Pancreatic cancer is the country's fourth leading cause of cancer death, killing over 32,000 individuals this year. Its 99 percent mortality rate is the highest of all cancers, and the average life expectancy after diagnosis with metastatic disease is just 3 to 6 months. The committee is pleased that the NCI

is moving forward to implement the recommendations outlined in the 2001 report by the Pancreatic Cancer Progress Review Group and that the Institute is funding three pancreatic cancer SPORE grants. However, the committee is concerned that the current level of funding for pancreatic cancer research does not allow for the implementation of the PRG report and that only one of the three SPORE grants is fully funded. In addition, the committee strongly urges the NCI to maintain or increase the number of pancreatic SPOREs as it undertakes a review of its translational research activities. Finally, the committee notes that the NCI's September 2004 report titled "Pancreatic Cancer Research" includes a single, overall budget figure for implementing the immediate and short-term strategies of the Institute's strategic plan to address the PRG's recommendations, with no details about how the money would be used. Therefore, the committee requests the NCI to develop a professional judgment budget that specifically details the cost of fully implementing the pancreatic cancer PRG and provide this professional judgment budget to the committee by May 1, 2006.

Prostate Cancer—The committee commends the NCI for the considerable investment in prostate cancer, the leading cause of non-cutaneous cancer death among men, and encourages NCI to continue to support research to improve the accuracy of screening and early detection of prostate cancer.

Radio Waves—The committee urges the NCI to support research using radio waves that could prove promising in reducing cancerous tumors. While current radio frequency ablation requires placing electrodes directly into the tumor, this new non-invasive technique would target only the cancer cells while avoiding healthy tissue.

Social Work—The committee encourages NCI to coordinate with the Centers for Disease Control and Prevention to conduct further research on the outcome of social work interventions to meet patient and family psychosocial needs in hospitals and cancer treatment centers.

SPORE Program—The Specialized Programs of Research Excellence Program at the NCI was established to support efforts to move laboratory findings into clinical practice to benefit patients in the near term. The committee understands that the program has resulted in the translation of some exciting research into cancer clinical trials for vaccines, chemoprevention and dietary interventions. The results to date from SPORE funding include multi-center clinical trials, biomarker studies, prevention studies, genetic registries, data sharing, and tissue banking projects, all with critical patient focus. The committee strongly encourages the NCI to continue to keep this translational goal at its forefront. The committee further understands that the SPORE program has been extremely successful in rapidly moving science to practices that benefit patients; funded research that requires a team approach to cancer; supports collaboration across basic science, population science and clinical investigation; and provides a rapid translation from the laboratory to patient care. The committee further urges that the translational research momentum, developed under the SPORE program, be maintained by the NCI.

Tuberous Sclerosis Complex—Tuberous sclerosis complex, or TSC, is a genetic disorder that triggers uncontrollable tumor growth in multiple organs of the body, including the brain, heart, kidneys, lungs, liver, eyes or skin. In light of its similarities to the uncontrolled growth of cancer cells, many scientists believe that determining the cause of tumor growth in TSC could open the way for cures and treatments for cancer as well. The committee is encouraged that NCI is participating in a Trans-NIH Tuberous Sclerosis Coordinating committee, and urges NCI's continued involvement in this process. The committee also urges NCI to collaborate with NIDDK on a conference on nutrient sensing and insulin-signaling in cells with inclusion of TSC research.

War on Cancer—The committee applauds the Director of the National Cancer Institute for setting a bold goal to eliminate suffering and death due to cancer by 2015. To assist Congress in establishing priorities, the committee requests the Director to report to the committee, by June 1, 2006, an outline of the progress made since the war on cancer was declared in 1971 and detail the specific steps that must be taken to achieve this goal by 2010.

Professional Societies:

Cancer Researchers Support Human Stem Cell Research

By Eric Lai

Three professional societies representing cancer researchers and clinicians support further "responsible" exploration in stem cell research to accelerate therapeutic developments for patients.

As debate over stem cell research continues in Congress and several state legislatures, the American Association for Cancer Research, the American Society of Clinical Oncology, and the American Society of

Hematology have drafted position statements addressing the issue.

"As the community of scientists on the front lines of the battle against cancer, we are firm in our belief that continued experimentation with human stem cells is necessary to improve evaluation of anti-cancer drugs, to identify markers for early detection of cancer, and to illuminate the path to novel, targeted treatments," said Lynn Matrisian, AACR past president and Ingram Distinguished Professor of Cancer Research at Vanderbilt University.

"Our belief is based on the results of peer-reviewed research, the strength of professional integrity and long-standing ethical principles, and profound respect for human life," Matrisian said in a statement AACR released July 13.

The organizations emphasized the potential of embryonic stem cells to transform into the cells of every major organ system in the human body. "If this characteristic can be controlled, then medical researchers could determine the signals that direct the development of human tissues, including cancers," AACR said.

Both ASCO and AACR approve of somatic cell nuclear transfer, also known as therapeutic cloning. SCNT involves transferring the nucleus of a cell from a patient into an egg whose cell nucleus has already been removed. The theoretical product of this process is an embryo with identical genetic and immune system profiles to those of the patient. Revealing the role of specific genetic alterations in tumorigenesis, further refinement of drug activity evaluations, and generating immune-compatible material for transplant therapies are just some of the promising developments that could come out of SCNT.

According to ASCO, slow progress has been made in regards to SCNT due to the concerns of ethicists over destroying embryos that have been created for research purposes. Most stem cell lines are derived from embryos left over from efforts to produce pregnancies. These embryos normally would be discarded, but these stem cells are generally not as flexible and adaptable as SCNT-derived stem cells.

The use of human reproductive cloning, or cloning to create a baby, was deplored by the organizations, and ASCO specifically found the practice to be "both unethical and medically inappropriate."

ASH and ASCO emphasized the need for expanding President Bush's 2001 list of human embryonic stem cell lines eligible for federal research funding. Out of the 78 embryonic stem cell lines that originally appeared eligible for federal funding under the policy, only 22 lines are actually available to investigators. Also, these lines are less than ideal for research due to possible contamination by the mouse cell media in which they were grown.

"The lack of stem cell lines eligible for federal funding has created roadblocks in this field and slowed medical and scientific progress," ASH said. "ASH firmly believes that with more human embryonic stem cell lines available for federal funding, new opportunities will become available for scientific advancement."

As a result of the fewer opportunities for federal funding in this field, American scientific prominence in stem cell research is at risk as private sector and foreign efforts gain more attention, said ASH.

Grant-making institutions should "work toward stable and sufficient funding for meritorious stem cell projects, free of political uncertainty, so that young investigators are encouraged to devote their careers to this important field," said William Nelson V, chairman of the AACR Science Policy and Legislative Affairs Committee and professor of oncology, urology, pharmacology and molecular sciences, medicine, pathology, and radiation oncology and molecular radiation sciences at Johns Hopkins University.

"Sadly, American stem cell biology suffers from a small and unsteady flow of graduate students, post-doctoral fellows and early-career faculty," Nelson said. "No scientific discipline can grow without the constant infusion of new talent and new ideas."

Obituary:

Daniel Martin, First To Combine Chemotherapy For Solid Tumors

By Eric Lai

Daniel Martin, a cancer surgeon and scientist who most recently was associated with Memorial Sloan-Kettering Cancer Center, died July 5 after being struck by a vehicle. He was 83.

Martin was credited for being the first scientist to combine different chemotherapy drugs to treat solid tumors in mice in the 1950s. After demonstrating that administering chemotherapy leads to tumor regression in transplanted breast cancer, Martin saw the research potential of mice which developed breast cancer spontaneously as a better model of study.

His work on adjuvant use of chemotherapy after surgery, published in 1962, preceded clinical application by more than 10 years, and is now the standard of care for patients with breast cancer.

"Long before the molecular biology revolution, he

saw the importance of combination chemotherapy for solid tumors as distinct from leukemias, and reported the first studies on this in transplanted Ca755 breast carcinoma tumors in mice," said James Holland, Distinguished Professor of Neoplastic Diseases at Mount Sinai School of Medicine. "He was a real pioneer with a clear vision."

Martin was born in Brooklyn, N.Y., in 1921. After graduating from New York University School of Medicine in 1944, he received further training at Harvard medical School and Columbia Presbyterian Medical Center. He was appointed director of research and chief of surgery at the University of Miami School of Medicine.

Returning to New York, Martin became chairman of the Department of Surgery at the Catholic Medical Center. He served as principal investigator for numerous NCI-funded projects that used early generations of mouse tumors. He held two NCI research contracts from 1972 to 1980, and a program project grant that was funded for 15 years. He published over 200 papers on his work, primarily on controlling the effects of known anti-cancer drugs to increase their effectiveness and decrease toxicity.

Two weeks before his death, Martin was awarded a research grant from NIH to investigate drug-resistant cancers. Based on his work with mouse models of human cancers, Martin believed that the combination of ATP depletion and standard chemotherapeutic agents could overcome the drug resistance problem, potentially leading to tumor regression. This was the subject of the new grant.

Martin is survived by his wife, Lisa; daughters, Danielle Martin, Gail Trano, Dee Martin, and Lee Martin; a son, Scott Martin; and three grandsons.

Cancer Prevention:

Smoking Deaths Cost Nation $92 Billion In Lost Productivity

Smoking cost the U.S. about $92 billion annually in the form of lost productivity in 1997-2001, up about $10 billion from the annual mortality-related productivity losses for the years 1995-1999, according to new data from the Centers for Disease Control and Prevention.

The new lost productivity estimate, when combined with smoking-related health-care costs, which was reported at $75.5 billion in 1998, exceeds $167 billion per year in the U.S.

The report also finds that during 1997-2001, an estimated 438,000 premature deaths occurred each year as a result of smoking and exposure to secondhand smoke. In comparison, approximately 440,000 smoking-related deaths were estimated to have occurred annually from 1995-1999.

"Cigarette smoking continues to impose substantial health and financial costs on individuals and society," said CDC Director Julie Gerberding. "We've made good progress in reducing the number of people who smoke, but we have much more work to do. If we want to significantly reduce the toll in this decade, we must provide the 32 million smokers who say they want to quit with the tools and support to do so successfully."

NIH Programs:

NIH Funds 11 High-End Instrumentation Grants

The National Center for Research Resources will provide nearly $18 million for 11 High-End Instrumentation grants that will fund the purchase of new state-of-the-art equipment to advance biomedical research.

The one-time grants support the acquisition of instruments that cost more than $750,000, with a maximum of $2 million each.

Instruments in this price range include structural and functional imaging systems, macromolecular nuclear magnetic resonance spectrometers, high-resolution mass spectrometers, electron microscopes, and supercomputers.

"Rapid technological development has led to a new generation of high-sensitivity, high-resolution instruments that are very expensive, but that can greatly accelerate research into the underlying mechanisms of disease," said Barbara Alving, acting director of NCRR. "The faster we can place these new technologies in the hands of as many NIH investigators as possible, the more rapidly we can transfer this new knowledge to patient treatments and cures."

Three or more NIH-funded investigators whose research requires the instrument must be identified in advance by the institution. Matching funds are not required, but institutions are expected to provide an appropriate level of support for associated infrastructure, such as building alterations or renovations, technical personnel, and post-award service contracts for instrument maintenance and operation.

The 2005 HEI Grants will be awarded to: Arizona State University; Cold Spring Harbor Laboratory;

Kennedy Krieger Institute Inc.; University of California, San Diego; University of Cincinnati; University of Maryland, Baltimore; University of North Carolina, Chapel Hill (two awards); University of Southern California; University of Virginia; and Washington University, St. Louis.

Funding Opportunities:

NCI RFA Available

RFA-CA-06-010: Ruth L. Kirschstein NRSA Fellowships in Cancer Nanotechnology Research

Application Receipt Date: Nov. 16

The RFA supports training from the basic, biomedical, clinical, and information sciences and engineering that applies nanotechnology development and application for the prevention, detection, diagnosis, or treatment of cancer. Nanotechnology offers an 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. As a result, nanotechnology will be a mission-critical tool to meet the NCI Challenge Goal of eliminating death and suffering from cancer by 2015.

The funding opportunity will use Ruth L. Kirschstein National Research Service Awards (Kirschstein-NRSA) to support individual postdoctoral fellowships F32 and senior fellowships F33.

The RFA is a component of the NCI Alliance for Nanotechnology in Cancer (http://nano.cancer.gov), an integrated 5-year initiative to develop and apply nanotechnology to cancer prevention, detection, diagnosis, and treatment, thereby enabling nanotechnology to become a fundamental driver of advances in cancer research and clinical oncology. The RFA is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-CA-06-010.html.

Inquiries: Gregory Downing, director, Office of Technology and Industrial Relations, Office of the Director, NCI, phone 301-496-1550; fax 301-496-7807; e-mail downingg@mail.nih.gov.

Program Announcements

PA-05-137: Etiology, Prevention, and Treatment of Hepatocellular Carcinoma R01 and R21

NCI and other institutes invite applications that address the etiology and etiologic mechanisms of hepatocellular carcinoma and development of animal models, approaches to prevent this malignancy, and therapeutic or diagnostic studies to establish prognostic indicators for disease progression and/or minimizing morbidity and mortality. Research activities are encouraged in the broad areas of etiology and etiologic mechanism(s) of liver cancer, including: identification of viral and host factors; development of animal models and in vitro viral cultivation methods; development of prevention and control strategies, including chemoprevention, validation of markers, and clinical trials of promising agents; and conduct of treatment and diagnosis research, including imaging studies. The types of mechanisms to be supported include traditional investigator-initiated R01 (individual) and R21 (exploratory/developmental) research grant applications. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-137.html.

Inquiries, for NCI: John Cole, Division of Cancer Biology, phone 301-496-1718; fax 301-496-2025; e-mail jc121b@nih.gov. Asad Umar, Division of Cancer Prevention, phone 301-594-2684; fax 301-435-6344; e-mail au17z@mail.nih.gov. Heng Xie, Division of Cancer Therapy and Diagnosis, phone 301-496-8866 or 301-496-6512; fax 301-480-4663; e-mail XieHe@mail.nih.gov .

PA-05-138: Etiology, Prevention, and Treatment of Hepatocellular Carcinoma P01

The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-138.html.

The funding opportunity involves use of the P01 grant award mechanism.

Inquiries: see preceding PA.

PAR-05-140: AIDS International Training and Research Program. Letter of Intent Receipt Date: Nov. 21, 2005, 2006, and 2007. Application Receipt Date: Dec. 21, 2005, 2006, and 2007.

Participating institutes, centers, including NCI, invite applications for collaborative training programs that would contribute to the goal of sustainable research capacity in HIV/AIDS and HIV-related conditions at institutions in low- and middle-income countries. The research-training programs will strengthen scientific knowledge and skills to enhance prevention of and treatment and care for HIV/AIDS and HIV-related conditions in these countries. The support is available through the D43 mechanism. The PAR is available at http://grants.nih.gov/grants/guide/pa-files/PAR-05-140.html.

Inquiries: Jeanne McDermott, Division of International Training and Research, Fogarty International Center, phone: 301-496-1492; fax 301-401-0779; e-mail mcdermoj@mail.nih.gov.

In Brief:

Mayo Scottsdale Opens New Research Building With TGen

(Continued from page 1)

Kennedy (D-Mass.) said these controversies, such as the withdrawal of Vioxx, wasn't Crawford's fault. FDA lacks funding and authority to do its work, Kennedy said. . . . **MAYO CLINIC** Collaborative Research Building, a research partnership between Mayo Clinic and Translational Genomics Research Institute, has opened on the Scottsdale campus of Mayo Clinic. The MCCRB provides a centralized set of resources for research into molecular medicine and genomics-based diagnostics and treatment methods. The $25-million biomedical facility will contain Mayo Clinic research business offices, investigational labs for hematologic malignancies, multiple myeloma and pancreatic cancer, the TGen Cancer Drug Development Laboratory and the TGen subsidiary, TGen Drug Development. The building was funded by developer **Tom Hornaday**. . . . **DANA-FARBER** Cancer Institute has established the Cancer Vaccine Center. The center is organized around two groups of core facilities, human immunology and clinical trials support, said **Ellis Reinherz**, director of the CVC. **Jerome Ritz** will oversee the clinical trials support cores, which are focused on vaccine manufacturing, clinical reagents and clinical and regulatory support. **Glenn Dranoff** will direct clinical trials. . . . **NEVADA CANCER** Institute made four staff appointments. **Nam Hoang Dang**, board certified in internal medicine and medical oncology, was named chief of hematological malignancies. **Yupo Ma** was appointed chief of hematology. He was director of flow cytometry, hematopathogist, and assistant professor in the Department of Pathology at the University of Arkansas Medical School. **Donald Hessel** is manager of imaging and radiology services. **Laura Bennett** was appointed director of grants and contracts. Bennett was director of Sponsored Programs and Research at Southeast Missouri State University at Cape Girardeau. . . . **ROBERT BLUMENTHAL** was named director of NCI's new Center for Cancer Research Nanobiology Program, which combines physics, computational sciences, and biology to develop nanoscale material-based strategies for the prevention, diagnosis, and treatment of cancer. The program, previously the Laboratory of Experimental and Computational Biology, will work with NCI's Nanotechnology Program, other CCR basic research labs and clinical branches, and the extramural community. . . . **MARK TALAMINI** was named chairman of the Department of Surgery, University of California, San Diego, School of Medicine and Medical Center. Talamini, known for his work in the use of robotics in laparoscopic surgery and a specialist in gastrointestinal disease, was professor of surgery and director of minimally invasive surgery at Johns Hopkins University School of Medicine. UCSD Medical Center will begin a robotic surgery program, beginning with a gastrointestinal surgery program, said Talamini. . . . **CLARA BLOOMFIED**, Ohio State University Cancer Scholar and senior adviser to the OSU Comprehensive Cancer Center, received the Charlotte Friend Memorial Lecture award from the International Association for Comparative Research on Leukemia and Related Diseases. . . . **LAURIE GASPAR**, professor and chairman of radiation oncology at the University of Colorado Cancer Center since 1999, was named the David F. and Margaret Turley Grohne Professor of Clinical Oncology. The $1.5 million endowment will be used to expand the radiation oncology clinical research program and build the radiation oncology fellowship program, said Gaspar. . . . **PETER WINKELSTEIN** was appointed chairman for clinical and scientific information at Roswell Park Cancer Institute. He was senior clinical informaticist at Eclipsys Corp. . . **JACQUELIN HOLLAND**, a registered nurse and program director in the Diversity Enhancement Program at the Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, was selected to serve as a consumer representative on the FDA National Mammography Quality Assurance Advisory Committee. . . . **STANTON GERSON** received the Mt. Sinai Health Care Foundation Maurice Saltzman Award on behalf of the Case Western Reserve University Comprehensive Cancer Center leadership team for their efforts to integrate cancer research in northeast Ohio. The award is given for work of significance or merit or of national or international importance to the health interests of the community. Members of the team include **Bryan Williams**, chairman, cancer biology, Lerner Research Institute; **Clark Distelhorst**, associate director for training and education; **Scot Remick**, associate director for clinical research and interim chief, hematology/oncology, Ireland Cancer Center; **Tena Rosner**, executive director and associate director for administration; **Kurt Stange**, associate director for prevention research; **Meri Armour**, director of clinical trials, and senior vice president, ICC; **Eric Klein**, section head, urologic oncology, Cleveland Clinic Foundation; and **Derek Raghavan**, director, Taussig Cancer Center, Cleveland Clinic Foundation.

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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