

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2009 Budget Request

Witness appearing before the
Senate Subcommittee on Labor-HHS-Education Appropriations

John E. Niederhuber, M.D., Director
National Cancer Institute

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Richard J. Turman, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

Thank you for the opportunity to offer testimony on behalf of the National Cancer Institute (NCI) and the National Cancer Program. The Fiscal Year (FY) 2009 budget of \$4,809,819,000 includes an increase of \$4,731,000 over the FY 2008 appropriated level of \$4,805,088,000.

A UNIQUE NATIONAL RESOURCE

At his hometown hospital, the patient remembers, “there were lots of debates and lots of questions about what I really had. They really didn’t know.” His condition was rare, and its identity remained elusive. Ultimately, one doctor made a simple promise: “I’m going to find somebody in this country that knows a lot more about this.” And so he did. Ten years ago, the patient headed to the National Institutes of Health Clinical Center in Bethesda, Md., and a research study lead by Dr. Wyndham Wilson at the National Cancer Institute. The condition turned out to be Lymphomatoid Granulomatosis, a rare, progressive disorder of the lymph nodes and blood vessels that can, over time, involve the lungs, skin, kidneys, and central nervous system. “If you look at the published literature on my disease,” the patient says, “it’s a very high mortality rate. What the NCI’s treatment regimen has done is completely turn that around. They’re doing things that other people just aren’t doing, and then sharing it and disseminating it throughout the world.” The patient remained in remission for 9 years. Last fall, when his disease returned, the patient returned to Dr. Wilson’s care with his optimism intact. “These people at the NIH are so talented, so kind — and they’re doing this just to help people and advance learning so that other people can benefit from their work around the country. They’re an amazing group of people.”

Our patient’s cancer story is not finished. Neither is the work of the National Cancer Institute. The NCI is striving for a time when the life stories of millions of patients will no longer end with cancer. For several years now, scientists who devote their careers to the study of cancer have spoken, with increasing frequency and enthusiasm, about their hopes for an era of “personalized medicine,” when cancer will be treated as a chronic condition — not the killer it is today. Spurred by the completion

of the landmark Human Genome Project, we have begun to realize a vision of cancer prevention, early diagnosis, and targeted treatment based on each patient's tumor and unique genetic make-up. In time, this knowledge will be linked to cancer risk and the earliest cellular changes that lead to development of a malignancy — years before tumor formation or symptom onset.

Today, cancer researchers are using new molecular technologies, such as whole genome scans and actual sequencing of patients' tumors, searching for abnormal proteins in individual patient's body fluids that are the result of these genetic changes. As a result, scientists are studying an ever-growing group of targeted therapies, which attack cancer cells but leave healthy tissue untouched.

Scientists have also learned the critical importance of the microenvironment of tissue surrounding the tumor, and they have elucidated the essential ways in which these cells — connective tissue cells, new blood vessel cells, and cells of the immune system — support the growth and metastasis of the cancer. Scientists have increasingly identified ways in which these non-cancer cells can also be targeted, to block tumor progression. Recognizing the complexity of a cancer and of its progression to a fatal disease, researchers have come to the understanding that our treatments will not be simple; complex therapies will help fight a complex disease. Without a doubt, science and the technology that supports research are making progress against cancer at a pace never before seen.

America's federal investment powers — and empowers — the engine of cancer research. The National Cancer Institute, as the leader of our National Cancer Program, funds thousands of researchers (5,713 in 2007) at hundreds of our great research universities and Cancer Centers from coast to coast — along with a cadre of government scientists based at the clinical center on the campus of the National Institutes of Health who, like Wyndham Wilson, conduct the kind of high-risk science unlikely to be found elsewhere.

Clearly, the nation's investment is paying dividends. There are now almost 12 million cancer survivors in America. Today's cancer research shows great promise to reduce the personal and financial costs associated with cancer, which, according to the American Cancer Society, totaled \$206.3 billion in the United States in 2006. However

of great worry, cancer is a disease of aging, the result of a lifetime of genetic alterations, additions, and subtractions that accumulate in our genes and impact their function. With a rapidly aging population, NCI estimates that the total economic burden of cancer in the United States will increase to \$1.82 trillion by 2017.¹ This clearly underscores the urgency of increasing our investment in cancer research. NCI's progress against cancer is evident across its vast research portfolio:

- **Genome-wide association studies** are revealing increasing numbers of genes that may contribute to cancer risk. These high-tech studies compare large groups of people: one group with a disease and one without, searching for abnormal genes, which, once validated and further studied, will lead to strategies for prevention, enhanced early cancer detection, and novel highly targeted treatments.

- **The NCI Community Cancer Centers Program**, now in a 3-year pilot phase at 16 sites across the country, is studying how best to bring state-of-the-art, multi-specialty cancer care, electronic medical records, and early-phase clinical testing of new therapies to patients in their own communities, because access to scientific advances is an essential factor in decreasing cancer mortality and healthcare costs.

- **The cancer Biomedical Informatics Grid (caBIG™)** is a 21st century information initiative connecting cancer research and clinical trials — both public and academic — from coast to coast. caBIG is an essential program to address the new era of highly personalized medicine and the rapid translation of discovery to practice.

- **Expanding deployment of Electronic Health Records** linked to clinical research can provide security and portability for patient health and medical information.

- **Pioneering a new kind of early clinical trial**, which looks at small numbers of patients and uses extremely small quantities of investigational medications and high-technology imaging, to see if the drug reaches its molecular target. Phase 0 trials have the potential to shorten drug development and reduce costs by millions of dollars.

- **NCI's expanding platform of new drug development** actively links university scientists with the complex enterprise of novel agent chemistry, validation, and the final steps of private sector translation.

¹ National Cancer Institute, Estimates of the National Economic Burden of Cancer for 2007 and 2017, April 17, 2007.

CANCER AS A MODEL OF DISEASE

Cancer has long been a model for the study of disease in the laboratory and a model of healthcare in the community. For example, knowledge about how tumors form new blood vessels (angiogenesis research), has contributed to our understanding of macular degeneration, diabetes, wound healing, and ischemic heart disease. In fact, the nation's investment in cancer research has affected the diagnosis and treatment of most major diseases. Cancer is the only disease for which tissue is routinely collected for study in the laboratory. Having malignant, pre-malignant, and normal tissue from the same patient allows researchers in many fields to understand the biology of pathologic disease processes, at the cellular level. The ability to perform tissue analysis also makes cancer patients the most highly characterized population of patients with chronic disease. Physicians are now using these data to inform prevention and treatment schemes tailored to the individual. The NCI recognizes that characterizing the patient and delivering state-of-the-art care in the community setting is the model for future healthcare delivery. We are continually studying ways to optimize this approach.

SUPPORTING RESEARCH

The backbone of America's cancer research enterprise is the individual investigator working at a laboratory bench, conducting hypothesis-driven science. These scientists are also the academic faculty who train and guide the next generation of researchers. Understanding those dual values, NCI is working to reassign resources to provide a stable level of financial support for Principal Investigators.

NCI is also pushing to reinvigorate its intramural program, comprised of the government scientists who study types of cancer unlikely to be addressed by the private sector and whose research encompasses high-risk science that has the potential to greatly advance our knowledge of cancer and its processes.

One of the greatest services NCI can offer the nation is to help foster a dedicated cancer research workforce for the future. We have placed more emphasis on carefully reviewing and more-aggressively funding new applications from young

scientists. We are working to bring more young scientists to Bethesda for day-long meetings and interactions with NCI staff. Moreover, because a grant from NIH is often a pre-requisite for obtaining and keeping academic tenure, NCI is developing plans to mandate a mentoring committee at each new investigator's home university.

WORKING FOR PATIENTS

When she arrived at the NIH Clinical Center, our patient couldn't even make a fist. Her hands, wrists, elbows, hands, and knees could scarcely bend. A once-vibrant woman in her late 20's, she was now severely anemic, wheelchair bound, and wrapped in blankets to preserve the body heat her skin could no longer retain. Over two years, as she suffered the disabling manifestations of cutaneous T-cell lymphoma, she spent more nights in the hospital than at home. She was in hospice care and lacked the strength to be with her two small children. She came to the Clinical Center virtually out of treatment options — and once there, an initial short list of experimental treatments had all failed. Having apparently run out of all hope, our patient came into the care of Dr. Martin E. Gutierrez, a staff clinician with the NCI's Medical Oncology Branch. Dr. Gutierrez, who has spent his career working on new therapies for T-cell lymphoma patients, tried a new drug being developed through NCI's Rapid Access to Intervention Development (RAID) program. RAID exists to speed the translation of novel anticancer therapies from laboratories to patients. And in this case, the new drug paid off dramatically. Within the first few doses, Dr. Gutierrez began to see improvement. Within seven months, the patient's symptoms were gone. Today, more than a year after her arrival at the Clinical Center, the patient's tests show no evidence of disease.

NCI will not rest until such stories are commonplace. Our nation's investment in cancer research is paying dividends — in lives saved, in greater quality of life for cancer patients, and in cancers prevented. The National Cancer Institute is dedicated to a future in which cancer is no longer the killer we know today, but a condition most often prevented, or else treated effectively, with minimal side-effects. The future of medicine is personal. Our country's investment in that future is vital. Everything we do at NCI begins and ends with real people: those with cancer, those at risk for the disease, and those who care for them.

Department of Health and Human Services
National Cancer Institute, National Institutes of Health
John E. Niederhuber, M.D., Director

John E. Niederhuber, M.D. became Director of the National Cancer Institute (NCI) in September 2006. Prior to that had had been the Institute's Acting Director, from June 2006. He was formerly the Wattawa Professor-Bascom in Cancer Research, Professor of Surgery and Oncology at the University of Wisconsin School of Medicine. Dr. Niederhuber served the University of Wisconsin as the Director of the University of Wisconsin Comprehensive Cancer Center from July 1997 until October 2002. He came to the University of Wisconsin in 1997 from Stanford University where he had served as Chair of the Department of Surgery. In June 2002, President George W. Bush appointed Dr. Niederhuber Chair of the National Cancer Advisory Board, a position he held until resigning to become the Deputy Director at NCI in 2005.

Dr. Niederhuber's research at the NCI focuses on the study of tissue stem cells as the cell-of-origin for cancer. His lab is working to identify, characterize fully and isolate this population of cells with the hypothesis that such cells might be the required therapeutic target. Under investigation, are the conditions that would make it possible to grow cancer stem cells in culture, such as hypoxia. Post transcriptional profiles of stem cells compared to other tumor cells and cells of the tumor microenvironment are being used to determine differences and potential drugable targets in cancer stem cells. Small interfering RNA (siRNA) technology is being used to reduce or block candidate gene expression. Tyrosine kinases and other cellular pathways, such as Hedgehog, in subpopulations of cancer stem cells compared to non-stem cells are used to further define unique targets. His lab is also studying the viral cancer vector HPV, to identify the binding site theorized to be a stem cell epithelial receptor.

The complex relationship between tumor cells and the microenvironment is another component of Dr. Niederhuber's research program. Studies will focus on how normal stroma is changed during tumor progression with the goal of developing strategies to prevent the development of tumors based upon an understanding of the alterations in the microenvironment. He holds a clinical appointment on the NIH Clinical Center Medical Staff.

Dr. Niederhuber is a nationally recognized cancer surgeon with a special clinical emphasis in gastrointestinal cancer, hepatobiliary cancer and breast cancer. He is recognized for his pioneering work in hepatic artery infusion chemotherapy and was the first to demonstrate the feasibility of totally implantable vascular access devices. The *Blk*-proto-oncogene was a novel discovery in Dr. Niederhuber's laboratory while he was a member of the faculty at The Johns Hopkins Medical School and is of interest because of its unique expression in B-cells and its participation in both proliferative and apoptotic pathways during B-cell differentiation.

Dr. Niederhuber has been a member of the Society of Surgical Oncology since 1978 and served as SSO President (2001-02). He also served as President of the American Association of Cancer Institutes (AACI) (2001-03). Dr. Niederhuber was

one of the founding members and served on the executive committee of the American College of Surgeons Oncology Cooperative Group. He was elected as an American Association for the Advancement of Science (AAAS) fellow in 2008.

He served as a member of the NCI Cancer Center's Review Committee (1984-86) and the NCI Division of Cancer Treatment Board of Scientific Counselors (1986-1991). He was Chairman of the Board from 1987-1991. He was a member of the NCAB Subcommittee to Evaluate the National Cancer Program (Committee to Assess Measures of Progress Against Cancer), chairing the Molecular Medicine Panel (1993-95). Dr. Niederhuber has served on the General Motors Cancer Research Foundation Kettering Prize Selection Committee (1988-89) and twice served on the GMCRF Awards Assembly (1988-92), (1998-02). He chaired the ASCO Surgical Oncology Task Force for the 2001-02 strategic planning process and the ASCO Public Policy and Practice Committee (2002-2003). He is a member of the Burroughs-Wellcome Foundation Translational Research Advisory Committee (1999-06).

Dr. Niederhuber is a graduate of Bethany College, Bethany, West Virginia and the Ohio State University School of Medicine. He was an NIH Academic Trainee in Surgery at the University of Michigan (1969-70) and a Visiting Fellow, Division of Immunology, The Karolinska Institute, Stockholm, Sweden (1970-71). He completed his training in surgery at the University of Michigan in 1973. He was a member of the faculty of the University of Michigan from 1973 to 1987, being promoted to Professor of Microbiology/Immunology and Professor of Surgery in 1980. During 1986-87, he was Visiting Professor in the Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine.

Dr. Niederhuber joined the faculty at The Johns Hopkins School of Medicine in 1987 as Professor of Surgery, Oncology, and Molecular Biology and Genetics. In 1991, He was appointed Emile Holman Professor of Surgery, Professor of Microbiology and Immunology and Chair of the Department of Surgery, Stanford University. He left Stanford in 1997 to become the Director of the University of Wisconsin Comprehensive Cancer Center where he has guided the consolidation of the University's two distinguished NCI supported cancer centers.

Dr. Niederhuber was recipient of a U.S. Public Health Service Career Development Award from NIAID (1974-79). In 1978 he received the Distinguished Faculty Service Award from the University of Michigan. He has also been recognized with the Alumni Achievement Award from The Ohio State University College of Medicine in 1989 and the Distinguished Alumni Award in Medicine from Bethany College (1995). In 2007, he also received an honorary Doctorate of Science from Bethany College. He was elected to *Who's Who in America* in 1998 and *Who's Who in Medicine and Health Care* (1997). In addition, he has received numerous honorary professorships and is currently serving on the editorial board of ten scientific journals. He was a member of the editorial board of the *Journal of Clinical Oncology* (1993-95). He has authored and coauthored more than 180 publications and edited four books, including, with distinguished colleagues, the highly regarded reference text *Clinical Oncology* which is currently in its third edition.

Department of Health and Human Services
Office of Budget
Richard J. Turman

Mr. Turman is the Deputy Assistant Secretary for Budget, HHS. He joined federal service as a Presidential Management Intern in 1987 at the Office of Management and Budget, where he worked as a Budget Examiner and later as a Branch Chief. He has worked as a Legislative Assistant in the Senate, as the Director of Federal Relations for an association of research universities, and as the Associate Director for Budget of the National Institutes of Health. He received a Bachelor's Degree from the University of California, Santa Cruz, and a Masters in Public Policy from the University of California, Berkeley