

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2012 Budget Request

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

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Mr. Chairman and Members of the Committee:

I am pleased to present the President's Fiscal Year (FY) 2012 Budget request for the National Cancer Institute (NCI) of the National Institutes of Health (NIH). The FY 2012 request includes \$5,196,136,000 for NCI, which reflects an increase of \$141,899,000 over the comparable FY 2011 level of \$5,054,237,000.

We now know that cancer is a collection of diseases reflecting changes in a cell's genetic makeup and thus its programmed behavior. Sometimes the genetic changes occur spontaneously or are inherited; sometimes they are caused by environmental triggers, such as chemicals in tobacco smoke, ultraviolet radiation from sunlight, or viruses. While cancers constitute an incredibly diverse and bewilderingly complex set of diseases, we have at hand the methods to identify essentially all of the genetic changes in a cell and to use that knowledge to rework the landscape of cancer research and cancer care, from basic science to prevention, diagnosis, and treatment. The funds in the President's budget for NCI represent a bold investment strategy critical for realizing that goal.

The emerging scientific landscape offers the promise of significant advances for current and future cancer patients, and for preventing cancer so that many never become cancer patients. And it offers scientists at the National Cancer Institute—and in the thousands of laboratories across the United States that receive NCI support—the opportunity to increase the pace of lifesaving discoveries dramatically.

In the past year alone, we have seen powerful examples of how research dollars have translated into concrete advances against cancer through basic science, prevention and early detection, and treatment.

Basic science. In collaboration with NHGRI, the NCI is leading The Cancer Genome Atlas (TCGA), the largest and most comprehensive analysis of the molecular basis of cancer ever undertaken. TCGA aims to identify and catalog all of the relevant genetic alterations in many types of cancer. For instance, building on their recent reclassification of glioblastoma multiforme (GBM), an aggressive form of brain cancer, this year TCGA investigators discovered that about 10 percent of patients with one of the four subtypes of GBM are younger at diagnosis and live longer than patients with other subtypes of the disease, but their tumors are unresponsive to current intensive therapies. The molecular profile of this subtype offers new targets for developing drugs to treat this form of the disease more effectively. TCGA scientists are also preparing to publish similarly important findings about the major form of ovarian cancer in mid-2011 and are in the midst of analyzing nearly 20 other types of cancer.

Prevention and early detection. NCI's intensive efforts to study and reduce the use of tobacco products have contributed to a sustained annual reduction in age-adjusted cancer mortality rates over the past decade and more. But current and former heavy smokers remain at high risk of developing lethal lung cancers, which are the leading cause of cancer mortality. In late 2010, NCI announced initial results from the

National Lung Screening Trial, a large, multi-year randomized trial that enrolled more than 53,000 subjects. Because early detection provides the potential to intervene at the earliest, most treatable stages of disease, thus reducing potentially difficult to treat outcomes seen in more advanced disease, current and former smokers who were screened with low-dose helical computed tomography were 20 percent less likely to die of lung cancer than were peers who received standard chest x-rays. These results provide the first clear demonstration that a screening procedure can be effective in reducing mortality from lung cancer—a finding that could save many lives among those at greatest risk. Over the course of the \$240-million study, NLST investigators collected samples of early and advanced lung cancers from enrolled subjects, and these specimens will be invaluable for determining genetic alterations that may be used to predict which tumors are likely to progress to an advanced stage.

Cancer treatment. The potential therapeutic impact of basic discoveries made by TCGA and other efforts in cancer genomics has been dramatically illustrated this year by the development of effective drugs against the most deadly form of skin cancer, melanoma. Almost a decade ago, studies of cancer genomes first uncovered a common mutation in a gene that encodes an enzyme called BRAF. Last year, early stage clinical trials at NCI-designated Cancer Centers of drugs targeted against the mutant BRAF enzyme showed that most melanomas with the relevant mutation regressed dramatically. Although tumor regression generally lasted less than a year, NCI-supported investigators have already pinpointed some causes of resistance to BRAF inhibitors, outlining a pathway to more sustained control of this lethal disease.

Another benefit of a prolonged and broad-based investment in cancer research has also been realized in the context of malignant melanoma this year, with the recent approval by the FDA of an antibody, ipilimumab, which extends the lives of patients with metastatic melanoma. Ipilimumab stimulates the immune system to act against cancer by blocking natural inhibitors of the immune response, an approach that would not be possible without a profound understanding of the immune system and one that promises to harness immunological tools against other cancers.

These examples of NCI's progress in understanding, treating, and detecting different forms of cancer illustrate what can be achieved at an accelerated pace with sustained investments across the cancer research spectrum, such as proposed under the President's budget. While those perspectives are only beginning to inform the American public's perception about cancer and its treatment, the downward trajectory of cancer deaths – reported by NCI and its partners in March -- reflects real and sustained reductions over more than a decade for numerous cancers, including the four most common: breast, colorectal, lung, and prostate. We have identified proteins and pathways that different cancers may have in common and represent targets for new drugs for these and many other cancers—since so often research in one cancer creates potential benefits across others.

Additional progress against cancer also will require building these research advances into clinical treatments and diagnostic tools for better patient care and by our many connections with public and private sector partners. The Institute's investments in translational research are broad and deep, and will receive NCI's full energies, recognizing that the publicly announced proposal for reorganizing services that support translational science in general could give NIH additional focus in this important area.

REVITALIZING THE CANCER CLINICAL TRIALS SYSTEM

For today's new understandings of cancer biology to benefit cancer patients on a broad scale, they must be coupled with a modernized system for conducting cancer clinical trials. This system must enable clinical researchers across the nation to acquire tumor specimens and conduct genetic tests on each patient, to efficiently analyze molecular changes in those samples, to manage and secure vast quantities of genetic and clinical data, and to identify subsets of patients with tumors that demonstrate changes in specific molecular pathways—pathways that can be targeted by a new generation of cancer therapies.

As part of its effort to transform the cancer clinical trials system, NCI asked the Institute of Medicine (IOM) in 2009 to review the Clinical Trials Cooperative Group Program. This program involves a national network of 14,000 investigators currently organized into nine U.S. adult Cooperative Groups and one pediatric cooperative group that conduct large-scale cancer clinical trials at 3,100 sites across the U.S. The IOM report, issued in April 2010, noted that the current trials system—established a half-century ago—is inefficient, cumbersome, under-funded, and overly complex. Among a series of recommendations, the report urged that the existing adult cooperative groups be consolidated into a smaller number of groups, each with greater individual capabilities and with new means to function with the others in a more integrated manner.

In December 2010, NCI announced its intent to begin consolidating the current nine adult cooperative groups into four state-of-the-art entities that will design and perform improved trials of cancer treatments, as well as explore methods of cancer prevention and early detection, enhance the ability of the cooperative groups to assess the molecular characteristics of individual patients' tumors, and study quality-of-life issues and rehabilitation during and after treatment. The sole pediatric cooperative group was created by consolidating four pediatric cooperative groups almost a decade ago, and that group will not be affected by the current consolidation effort.

PROVOCATIVE QUESTIONS

This has been a challenging and hopeful time for NCI to lead the nation's cancer research program. Over the past two decades researchers have unraveled some of the damage that occurs in the genome of a cancer cell and how a cancer cell behaves in its local environment as a result of those changes. With this better understanding of cancer and recent technological advances in many fields, such as genomics, molecular biology,

biochemistry, and computational sciences, progress has been made on many fronts, and a portrait has emerged for several cancers. With sustained and accelerated funding, and NCI's strong leadership in defining cancer research priorities, we can build upon today's cancer advances with provocative thinking by asking better questions.

To that end, NCI is asking researchers in various disciplines to pose and articulate "provocative questions" that can help guide the nation's investment in cancer. Provocative questions may be built on older, neglected observations that have never been adequately explored, or on recent findings that are perplexing, or on problems that were traditionally thought to be intractable but now might be vulnerable to attack with new methods.

Many of these provocative questions are being asked – and answered – by young scientists who are early in their careers. The 2012 budget will support NCI's commitment to ensuring that an equitable share of our research grants will go to the young men and women, who are at the forefront of understanding cancer.

We are now reaping the rewards of investments in cancer research made over the past 40 years or more, even as we stake out an investment strategy to realize the potential we see so clearly for the future. The public has benefitted from past generous Congressional stewardship of biomedical research funding; cancer research over the past four decades has provided the evidence required to lower the incidence and mortality of many kinds of cancer, to improve the care of cancer patients, and to establish the new understanding of cancer that is now beginning to revolutionize control of cancer throughout the world.

No matter what the fiscal climate, NCI will strive to commit the resources necessary to bring about a new era of cancer research, diagnosis, prevention, treatment, and survivorship.

Thank you for the opportunity to provide you this testimony, and I would be pleased to answer any questions you might have.

HAROLD VARMUS, M.D.
DIRECTOR, NATIONAL CANCER INSTITUTE

Harold Varmus, co-recipient of the Nobel Prize for studies of the genetic basis of cancer, became Director of the National Cancer Institute on July 12, 2010, after 10 years as President of Memorial Sloan-Kettering Cancer Center, following six years as Director of the National Institutes of Health. He is a member of the U.S. National Academy of Sciences and the Institute of Medicine and is involved in initiatives to promote science in developing countries, including the Global Science Corps. The author of over 350 scientific papers and five books, including a recent memoir titled The Art and Politics of Science, he was a co-chair of President Obama's Council of Advisors on Science and Technology, was a co-founder and Chairman of the Board of the Public Library of Science, and chaired the Scientific Board of the Gates Foundation Grand Challenges in Global Health. In 2001, he received the National Medal of Science.