National Cancer Institute

The Nation's Investment in Cancer Research

Connecting the Cancer Community

An Annual Plan and Budget Proposal for FY2009

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

FOREWORD: DIRECTOR'S INTRODUCTION

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

Jeanne McCoy's grandmother and mother both suffered from von Hippel-Lindau syndrome 60 (VHL), a genetic disease that can manifest itself as a combination of nearly 600 types of cancer. For Jeanne's grandmother, the tumors appeared first on her retina (she went blind at the age of 30) and also on her brain stem. Eventually the cancer invaded her kidneys. Jeanne's mother, who was told at a young age that she did not have VHL, was shocked to learn later in her life that this diagnosis was wrong. That family history led Jeanne to search the Internet, where she learned of the recently-identified VHL gene. Jeanne sought out the National Cancer Institute, where Dr. Marston Linehan was leading a team of researchers who were working at the cutting edge of VHL—both in the laboratory and in the clinic.

Because of the late stage of her cancer and her family history, Jeanne's mother was quickly accepted into the clinical program at the NCI. There, she was confirmed to carry the VHL mutation. Several months later, Jeanne sent her own blood sample and records to NCI. The results confirmed that Jeanne also carried the VHL mutation.

Jeanne had no symptoms of kidney cancer. In fact, at age 34, she had given birth to her third child a year earlier. Except for faint back pain, something many new mothers experience, Jeanne felt fine. But she also knew that the VHL mutation suggested a frightening fate. So Jeanne consulted her local oncologist, who advised her to undergo an ultrasound and CT-scan in a hospital near her Greenville, South Carolina, home. Within hours, she learned that both her kidneys were riddled with cysts and tumors that, if untreated, would eventually kill her.

Within two weeks, Jeanne was headed for Bethesda, for more testing and consultation, and treatment at the National Cancer Institute. While hospitalized for the second of her kidney surgeries, just before Christmas 2003, Jeanne met Dr. Linehan, who came to see her in the surgical intensive care unit at the NIH Clinical Center, the world's largest hospital dedicated to clinical research. "He sat down and talked to my husband and me," she recalls. "And suddenly he put a real, personal face on the research; we realized that this wasn't about scientists lost in a lab, it was about people, and about early diagnosis and detection, and about finding a cure."

Jeanne McCoy is doing well, but she is not cured. All of us owe a huge debt of gratitude to her and many other cancer patients for their willingness to join us in defeating this devastating disease, by participating in clinical research

NCI Strategic Objectives

To Preempt Cancer at Every Opportunity

- Understand the causes and mechanisms of cancer.
- Accelerate progress in cancer prevention.
- Improve early detection and diagnosis.
- Develop effective and efficient treatments.

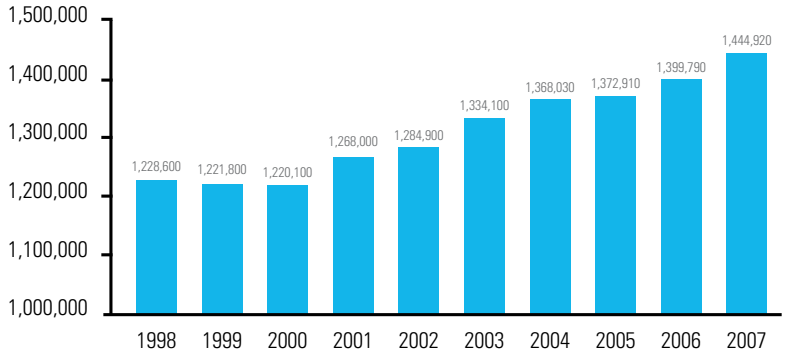
To Ensure the Best Outcomes for All

- Understand the factors that influence cancer outcomes.
- Improve the quality of cancer care.
- Improve the quality of life for cancer patients, survivors, and their families.
- Overcome cancer health disparities.

Why It's Important: the Human and Economic Burden of Cancer*

- 1,444,920 Americans were diagnosed with cancer in 2007
- 559,650 Americans died of cancer in 2007
- $206.3 billion was spent on healthcare costs for cancer in 2006

Estimated Number of New Cancer Cases in the United States from 1998 to 2007



*Data source: American Cancer Society, Cancer Facts and Figures, 1998 to 2007 based on NCI SEER and NAACCR data.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and trials. For the sake of Jeanne and her family, and the countless others like them, we need to make more progress more quickly.

Everything we do at NCI begins and ends with people—those with cancer, those at risk for the disease, and those who care for them. That singular focus lies at the heart of all our work in basic, translational, and clinical science to better treat cancer; our outreach into communities across the United States; and our efforts to build cancer prevention strategies and programs. People with cancer are not just "patients" to us. They are human beings with family, friends, dreams, and lives that are all impacted by their diagnoses. Cancer patients are the cornerstone of cancer research, and we are forever indebted to those men and women who give so generously of themselves to make life better for others.

Cancer, as a disease, is incredibly complex, both in its biology and in its social impact. We now know that cancer is not a single disease or even a small group of related diseases. Rather, we are finding that when viewed at the level of genes and proteins, cancer is a collection of many different diseases. It is this greater understanding of cancer at the molecular level that NCI believes will enable us to change the meaning of a cancer diagnosis in the future. The National Cancer Act of 1971 established the National Cancer Program and authorized NCI to coordinate its efforts. Encompassing academia, industry, the private sector, international partners, and other government agencies, NCI directs a massive multifaceted effort against cancer that continually strives to match the enormity of the disease itself.

NCI is dedicated to the understanding, diagnosis, treatment, and prevention of cancer for all people. To these ends, NCI creates connections: basic science to clinical therapies; researchers to patients and doctors; NCI internal ("intramural") work and external ("extramural") efforts; public and private cancer-related institutions and research; and the U.S. effort to the wider global fight against cancer.

We have made progress, but much work remains. The rate of cancer mortality continues to drop; however, cancer still remains a leading cause of death, second only to heart disease. The number of new cancer diagnoses continues to rise, with more than 1.4 million people hearing the dreaded words "you have cancer" this year in the United States alone. And we know this burden is disproportionately shouldered by the poor, the elderly, and minority populations.

Our progress is thanks to the work of thousands of cancer researchers, both at the lab bench and in the clinic, and numerous patients who seek not only treatment for themselves but also to provide hope for others. As we now understand that cancer is a disease that results from changes in our genes, we are striving to comprehend the precise changes that occur before we are born or as we interact with our environment, and how to prevent or overcome them. We have pried open some of the secrets of how cancer begins, how it takes advantage of our normal biological makeup, and how it initiates its lethal spread, and we are pursuing potential new avenues to learn to stop it in its tracks.

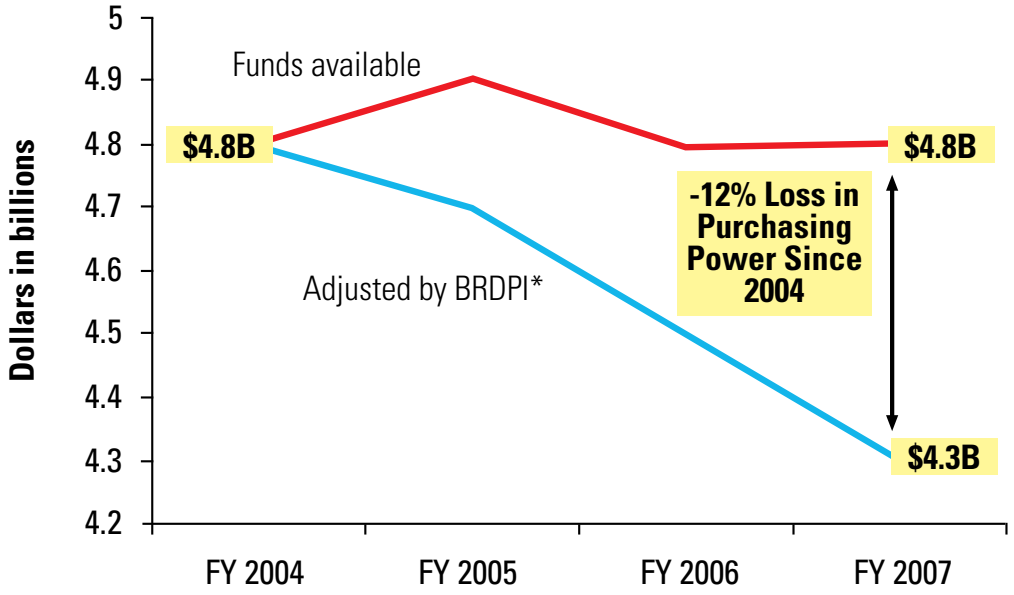
Each step forward we take opens up promising new opportunities to make further progress, which must be seized. NCI cannot do this alone. Thus, it is essential that NCI increase its capacity to enable and support the many critical connections that will bring about real changes in cancer prevention, diagnosis, and treatment, all the while ensuring that the latest scientific advances become available to all patients, not just those who have access to the NIH Clinical Center or other leading national cancer centers.

Making these connections is not an easy task, and it is made even more difficult in light of the budgetary realities we face. Nearly 80 percent of our annual funding goes to support external scientists and researchers at academic institutions and centers across the country, including many who conduct the clinical trials necessary to translate basic scientific findings into cancer treatments. Much of the remainder supports our internal research operation, which facilitates collaborative opportunities between world class scientists, both at NCI and elsewhere, provides freedom to pursue new insights and opportunities (particularly for underserved populations), and trains and develops the next generation of cancer researchers.

The below-inflation budgets of the last two years have impacted both our internal and external capabilities. Indeed, implications of our budgetary constraints have carried beyond the basic research laboratories, impacting the clinical research options available to patients. For example, the NCI's Clinical Trial Cooperative Groups, which promote and support clinical trials of new cancer treatments, explore methods of cancer prevention and early detection, and study quality-of-life issues and rehabilitation during and after treatment, saw their funding cut by 10.9 percent between fiscal year 2002 and 2006. Although some of their lost funding was restored in FY 2007, fewer trials have been started, and fewer patients have been enrolled in available trials. This slows our ability to improve the standard of care for cancer patients through new drugs, devices, or interventions.

Between the fiscal years 2004 and 2007, NCI's budget remained relatively flat. However, factoring in the rate of

NCI'S CHALLENGE



* BRDPI: Biomedical Research and Development Price Index

[http://officeofbudget.od.nih.gov]

The NCI is a unique national resource, one that can bring together the various aspects of the National Cancer Program by acting as a convener and facilitator of the public and private sectors to deliver on the promise that was made by the National Cancer Act of 1971.

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biomedical inflation reveals a 12 percent loss of purchasing power over those same years. Investigators tell us that below-inflation funding often means the loss of a laboratory technician or two, a graduate student not brought into the lab, a postdoctoral fellow not hired, or research that must be scaled back to the point that scientific progress is significantly slowed and some opportunities are lost. The problem is compounded because these investigators—some of whom are turning away from biomedical science—are also the professors who nurture the careers of young scientists who will drive the future of cancer medicine.

Aware of the fiscal situation we face, this document is a report on progress and opportunities, as well as a plan for critical scientific growth. It details the state of our science, the extraordinary promise of today's research, and the resources we believe would allow NCI to hasten the day that the promise of personalized cancer medicine arrives. That day will also usher in a new era of cancer prevention, with new diagnostic tests that can predict the impending development of cancer long before the formation of a tumor.

The NCI is a unique national resource, one that can bring together the various aspects of the National Cancer Program by acting as a convener and facilitator of the public and private sectors to deliver on the promise that was made by the National Cancer Act of 1971. The nurturing and careful stewardship of this national resource is our shared responsibility. Cancer touches virtually every American family, and NCI is committed to research that helps us provide access to the best standard of care for all in the communities where they live and work. And it is on behalf of every cancer patient that NCI will continue its vital research, until stories about successful battles against cancer are the only ones to tell.

I. EMPOWERING CANCER RESEARCH.

Every life is touched by cancer. As the leader of the U.S. efforts to understand, diagnose, treat, and prevent cancer in all of its forms, NCI must play the central role in bringing together basic and clinical researchers, patients, physicians, care givers, policy makers, and many others in a common cause.

The convergence of new biomedical technologies with information technologies has revealed to us just how complex cancer truly is. Indeed, the biology of cancer is intimately intertwined with the unique genetics of each person, making it an "individualized" disease. The ability to deliver individualized interventions to patients requires the integration and collaborations of disciplines not traditionally thought of as part of cancer research. This broader view of the cancer research community extends to mathematicians, physicists, and chemists as well as others in the physical sciences and relies on their skills and talents to enhance our ability to manage large amounts of data as well as developing novel applications in clinical research.

THE PROMISE OF PERSONALIZED CANCER MEDICINE

The progress we have made has opened up a vision of a future personalized cancer medicine, when doctors will determine prognosis and treatment options by understanding each patient's unique genetic makeup and the genetic aberrations that have led to his or her cancer. That future includes developing combinations of therapeutic solutions that target the multiple pathways of cancer, earlier interventions that eradicate cancer long before the development of a tumor or the onset of symptoms, and effective prevention methods based on the individual.

Personalized Cancer Medicine

Detection and diagnosis

- Identify patterns of genes associated with the development of specific cancers.
- Study how genetic variations that change the function of proteins cause cells to function abnormally. Investigate how those changes are further affected by lifestyle behaviors and environmental factors.
- Develop biomarkers—blood tests and other tests using human specimens; imaging techniques; and other new methods—to detect and measure changes in protein and cellular function associated with specific cancers.

Prognosis and prevention

- Monitor the changes in an individual's cellular function, in order to detect pre-cancerous changes and intervene to prevent those changes from progressing to disease.
- Use genetic profiles to identify subsets of cancer types that define prognosis.

Treatment

- Choose targeted therapies that minimize side effects and are based on both the type of cancer and the individual's biological profile.
- Use biospecimen tests and imaging techniques to measure the impact of interventions and refine treatment to improve outcomes.

In a development that is literally lifesaving, Dr. Staudt, who has been on the staff of NCI for nearly 20 years, has successfully used genomic technology to reliably distinguish Burkitt's lymphoma from Diffuse Large B-Cell Lymphomas (DLBCL).

Louis M. Staudt, M.D., Ph.D., and members of his NCI laboratory

This is a vision shared across the oncology research community. The NCI-designated Cancer Centers Directors' report "Accelerating Successes Against Cancer"* also recognizes that advances in treatment will come from understanding molecular causes of disease and using combination treatment approaches employing multiple modalities. The National Cancer Institute has not only embraced but is leading the way to that future, and is dedicated in all it does to ushering it in as rapidly as possible.

THE ESSENTIAL UNITY OF BASIC AND TRANSLATIONAL SCIENCE

In addressing the burden of cancer, there is an essential unity between fundamental scientific studies on the molecular causes of cancer, research focused on translating those studies into the clinic, and actual clinical practice. The traditional linear relationship from the bench to the bedside is no longer an effective and efficient model for medical progress. Insights from fundamental scientific research need to be tested in clinical settings, which in turn give rise to new research directions that can be pursued in the laboratory.

Indeed, at the NIH Clinical Center and at many other cancer research and treatment centers across the country, laboratories and patient rooms are in close proximity. Cancer researchers within NCI and based at other institutions are committed to working together to mine new insights from wherever they arise for truly effective cancer treatments.

ON THE FRONT LINES: CONNECTING SCIENCE AND CLINICAL PRACTICE "CASE STUDIES"

Louis M. Staudt, M.D., Ph.D., studies lymphoma, a cancer of the lymphatic system that affects 23,000 patients yearly and causes 10,000 deaths Treatment can be difficult, because this cancer has many subtypes, which require different treatment options. For example, Burkitt's lymphoma and diffuse large-B-cell lymphoma (DLBCL) are difficult to diagnose because the two cancers appear very similar under a microscope. However, the two are genetically distinct, and thus require very different treatments.

And the stakes couldn't be higher. "If Burkitt's patients are treated with intensive therapy, there is roughly an 80 percent survival rate," says Dr. Staudt, deputy chief of the Metabolism Branch and head of the Molecular Biology of Lymphoid Malignancies Section in NCI's Center for Cancer Research. "However, if they are misdiagnosed and treated with the lower intensity chemotherapy recommended for DLBCL, the survival rate is 20 percent or even less."

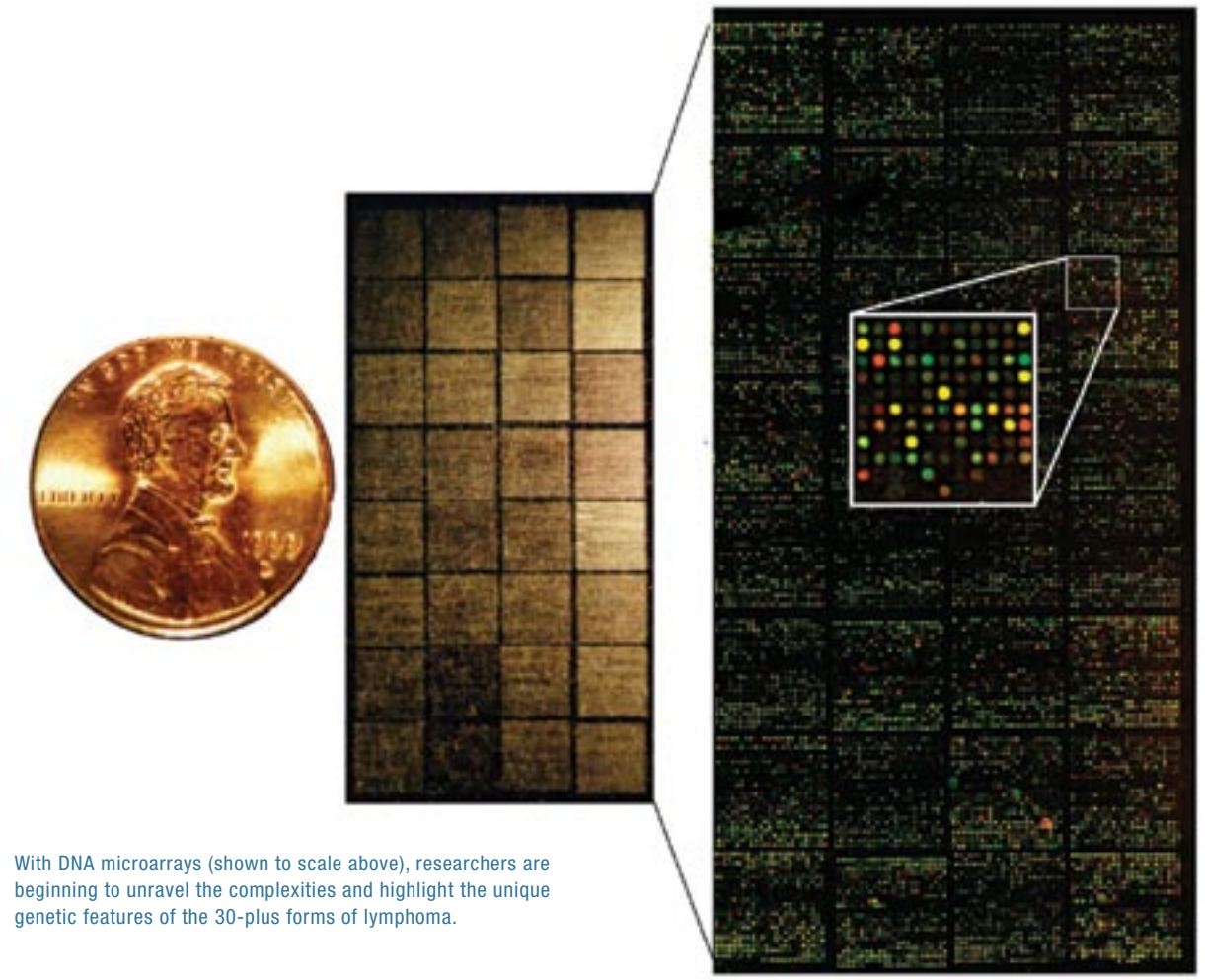
In a development that is literally lifesaving, Dr. Staudt, who has been on the staff of NCI for nearly 20 years, has successfully used genomic technology to reliably distinguish Burkitt's lymphoma from DLBCL. Dr. Staudt demonstrated that DNA microarrays, a technology rooted in the

* [NIH Publication No. 06-6080, September 2006]

Human Genome Project, can accurately distinguish Burkitt's lymphoma from DLBCL, thereby optimizing the treatment choice for each patient. "The current goal with the improved diagnostics technology is to make it uniform, reproducible, and available as a cost-effective test," notes Dr. Staudt.

In collaboration with a private sector company, researchers are now enrolling 2,000 to 4,000 patients for a large study of a new test designed to distinguish between all types of lymphomas and other, benign conditions.

Even as work continues on better diagnostics, Dr. Staudt points out that improved lymphoma treatments are also being discovered. Dr. Wyndham Wilson, a clinician at the NIH Clinical Center, has developed a novel, less toxic form of chemotherapy to treat Burkitt's lymphoma, called dose-adjusted EPOCH-R. In this treatment, the dosage of chemotherapeutic drugs is increased with every cycle until a maximum tolerated dosage is reached. "It's an empirical way of adjusting the dosage to fit each patient, which avoids both under treatment and over treatment," says Dr. Staudt. "This approach adjusts for differences in metabolism, age and genetics that can influence a patient's response to drugs."

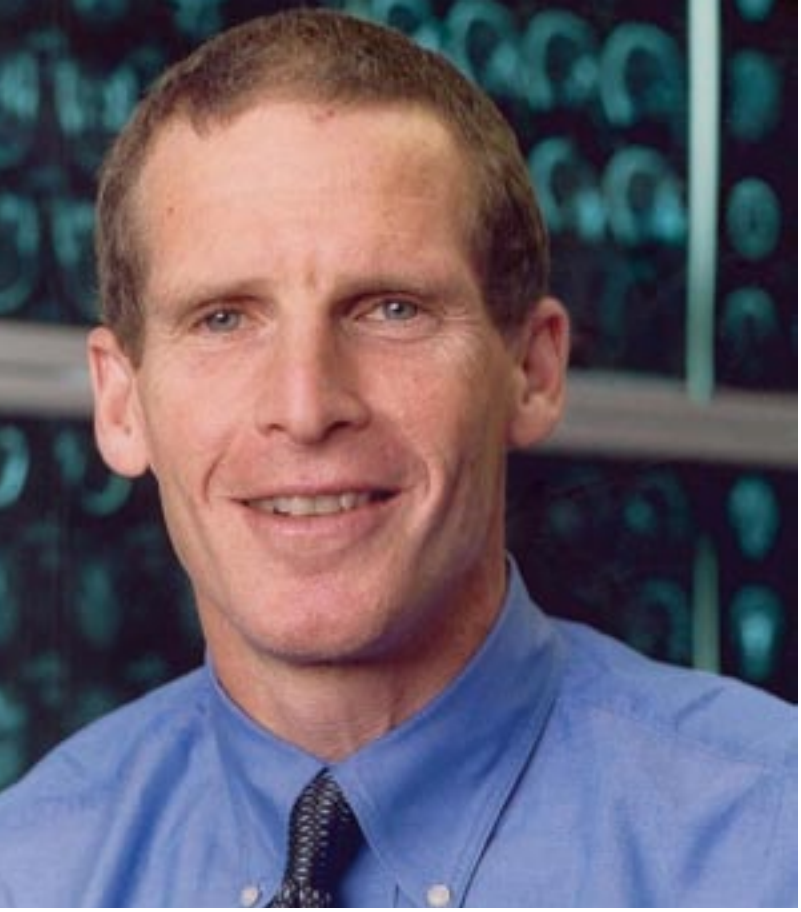


With DNA microarrays (shown to scale above), researchers are beginning to unravel the complexities and highlight the unique genetic features of the 30-plus forms of lymphoma.

Louis Staudt, NCI

Lymphoma Genomic Profiling

The Lymphoma/Leukemia Molecular Profiling Project (LLMPP) is a network of 11 clinical groups that maintain biospecimens and clinical data from hundreds of patients with this cancer of the lymphatic system. An international consortium of investigators, including NCI-funded investigators and researchers around the world, the LLMPP is classifying lymphoma by distinct molecular characteristics and is then using that information to more accurately guide diagnosis and to target treatment.



Howard A. Fine, M.D., Chief of the Neuro-Oncology Branch at NCI's Center for Cancer Research

Dr. Howard Fine "sees as many patients as want to see me." As the Chief of NCI's Neuro-Oncology Branch, he evaluates between 2,000 and 3,000 brain tumor patients a year. Brain cancer, he says, "is a disease that impacts patients physically, while eroding their cognition and personality, exacting a devastating toll on both the patient and caretaking families." Unfortunately, as Dr. Fine points out, "the current standard of care is not optimal." The disease is not amenable to prevention or early diagnosis, and care for brain cancer patients falls between the expertise of neurology and medical and surgical oncology. Dr. Fine is committed to changing that situation.

Gliomas are the most common tumors that originate in the brain, beginning in the cells that surround and support nerve cells. Patients with low-grade glioma, which tends to grow more slowly, have a survival rate that averages 5 to 10 years, while patients with high-grade, or aggressive, glioma (glioblastoma being most common) have a 14-month survival rate. The standard treatment for glioblastoma is surgery, radiation, and chemotherapy. Dr. Fine explains that glioblastomas are "hugely different" from patient to patient, which makes the case for a better understanding of the underlying genetic abnormalities that distinguish one type from another. Although several key genes have been shown to play a role in glioblastoma, and drugs that inhibit these targets have been developed, many other genes remain to be identified.

Dr. Fine envisioned an integrated program to study large numbers of glioma patients—comprised of 20 NCI-designated Cancer Centers, the pharmaceutical industry, brain tumor consortia, clinical trial cooperative groups, and other NIH Institutes. His concept, the Glioma Molecular Diagnostic Initiative, or GMDI, collects and correlates standardized data from tumor specimens that can be analyzed to identify patient genetic profiles and novel molecular targets—and to help develop patient-tailored therapy. For Dr. Fine, efforts such as this "represent a flagship initiative that brings together divergent programs in a war that couldn't be won otherwise."

HARNESSING THE POWER OF NEW TECHNOLOGIES TO UNDERSTAND, DIAGNOSE, TREAT, AND PREVENT

Building upon the successful completion of the Human Genome Project and applying its insights to cancer diagnosis, treatment, and prevention will require new tools that empower and connect the entire cancer enterprise. In addition to traditional single investigator/laboratory projects, NCI supports large projects that involve multi-disciplinary and multi-institutional teams of scientists. Both types of projects play critical and interconnected roles towards a single goal: rapidly translating new findings into effective new clinical practices.

Diagnosing Brain Cancer

NCI's Glioma Molecular Diagnostic Initiative (GMDI) aims to develop a comprehensive molecular classification system for this type of brain cancer, thus allowing consistent prediction of response to therapies for individual patients. The largest study ever conducted to merge genetic and clinical information, GMDI is a nationwide partnership of several NIH Institutes and NCI-funded consortia and scientists. GMDI investigators are conducting retrospective studies, which look backward to examine exposures to suspected risk, and prospective studies, which watch for outcomes over a long period of time, to build and validate molecular and genetic models of glioma. The molecular, genetic, and clinical data from GMDI are being compiled in REMBRANDT (REpository for Molecular BRAin Neoplasia DaTa), a publicly accessible online database and universal classification system.

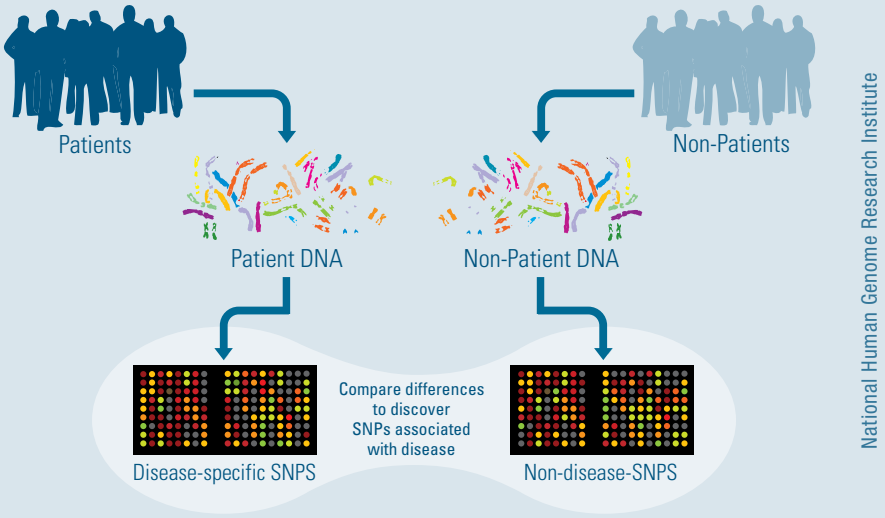
GENETICS OF CANCER

Deciphering the human genome sequence was a watershed event early this decade, providing a fundamental blueprint for beginning to understand the genetic contributions to human health and disease, including cancer. However, what truly matters is to understand the effects of various differences on an individual's risk of developing cancer, on drug effectiveness for their tumor, and on their susceptibility to side effects. These genetic changes can also be used as markers for monitoring the progression of cancer. Although the technology for sequencing each person's genome remains prohibitively expensive, the work of many scientists—including those at NCI—has resulted in a catalog of common genetic variations across the human population (The International HapMap) that can be used as "landmarks" to quickly identify genetic elements relevant to cancer and therapy.

This new approach, known collectively as Genome-Wide Association Studies (GWAS), is resulting in a flood of data about the underlying molecular contributions to different forms of cancer and other diseases, and it is opening up exciting new opportunities for discovering and developing therapeutic interventions that go to the root causes rather than just the symptoms of cancer.

NCI is leading the application of this exciting new technology, known as whole genome association studies, to cancer in several different initiatives, including:

The Cancer Genetic Markers of Susceptibility (CGEMS) Initiative: Initiated in 2005, CGEMS is a collaborative team of several research groups performing GWAS on the DNA of patients with prostate or breast cancer and comparing the results to those from patients without cancer. The results from this work are freely available to researchers around the world to facilitate further study of the biological basis of cancer and also as the basis for new methods of diagnosis, intervention, and prevention of cancer.



GWAS Explained: How Are Genome-Wide Association Studies Conducted?

To carry out a genome-wide association study, researchers analyze the DNA of two groups of participants: people with the disease being studied and similar people without the disease. Each person's complete set of DNA, or genome, is placed on tiny chips and scanned on automated laboratory machines, which quickly survey each participant's genome for strategically selected markers of genetic variation, which are called single nucleotide polymorphisms, or SNPs.

If certain genetic variations are found more frequently in people with the disease compared to people without disease, the variations are said to be "associated" with the disease. The associated genetic variations can serve as powerful pointers to the region of the human genome where the disease-causing problem resides.

However, the associated variants themselves may not directly cause the disease. They may just be "tagging along" with the actual causal variants. For this reason, researchers need to take additional steps, such as sequencing DNA base pairs in that particular region of the genome, to identify the exact genetic change involved in the disease.

Genome-Wide Association Studies: Progress and Opportunities

Genome-wide association studies involve rapidly scanning a collection of known genetic markers across the complete genomes of many people to find genetic variations that are associated with a particular disease. By using regularly spaced genetic markers across the genome, researchers can rapidly hone in on areas that are altered in people with a particular form of cancer, identify the specific genetic changes, and develop better strategies to detect, treat, and prevent the disease.

The Cancer Genome Atlas (TCGA): TCGA, a joint effort by NCI and the National Human Genome Research Institute (NHGRI), is a coordinated research initiative to develop a comprehensive catalog, or atlas, of the many genetic changes that occur in cancers, from chromosome rearrangements, to DNA mutations, to epigenetic changes (the chemical modifications of DNA that can turn genes on or off without altering the DNA sequence). The potential of a cancer genome "atlas" is tremendous, enabling detection of disease early when it is curable, distinguishing which patients will respond to therapy, providing new targets for drug development, and ultimately providing prevention strategies for people at risk for developing cancer. The TCGA Pilot Project is currently focused on three types of cancers: brain (glioblastoma multiforme), lung (squamous carcinoma), and ovarian (serous cystadenocarcinoma), which together account for more than 210,000 cancer cases each year in the United States alone. Data derived from these studies are rapidly made freely available for the use of cancer researchers everywhere.

Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments (TARGET) Initiative: The TARGET Initiative, a joint venture of NCI and the Foundation for NIH, is a public-private partnership to identify and validate therapeutic targets so that new, more effective treatments can be developed for children with cancer. Its immediate goal is to make major advances in identifying and validating therapeutic targets beginning with acute lymphoblastic leukemia and neuroblastoma. The TARGET initiative builds upon the experience and expertise NCI has gained in working with the NHGRI to build The Cancer Genome Atlas. TARGET will comprehensively characterize genomic profiles of selected childhood cancers and utilize DNA sequencing to identify those specific genes that are consistently altered in those cancers. Finally, high throughput screening methods that can rapidly identify active compounds, antibodies, or genes that modulate a particular biomolecular pathway will be applied to identify and validate therapeutic targets.

Daniela S. Gerhard, Ph.D.

Director, NCI's Office of Cancer Genomics

Dr. Daniela Gerhard was appointed Director of the Office of Cancer Genomics at the National Cancer Institute in 2005. Among her responsibilities in overseeing many of NCI's cancer genetics programs are her role as the project director of the Cancer Genetic Markers of Susceptibility (CGEMS) project, and serving as a member of The Cancer Genome Atlas (TCGA) management staff. She says, "For the first time, we have the tools to truly understand and address the fundamental causes of cancer, and make a profound difference in the lives of cancer patients everywhere."

Dr. Gerhard is a well-known human geneticist and molecular biologist. Her previous work at Washington University School of Medicine in St. Louis included identifying the key issues in the genetically complex bipolar affective disorder, the physical and genetic mapping of human chromosome 11, the cloning of the gene for multiple endocrine neoplasia, type 1 (located on chromosome 11), evaluation of genetic risk factors in prostate and cervical cancers, and the identification of a candidate region that harbors a gene relevant to cervical cancer development.

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

UNDERSTANDING THE BIOLOGY OF CANCER

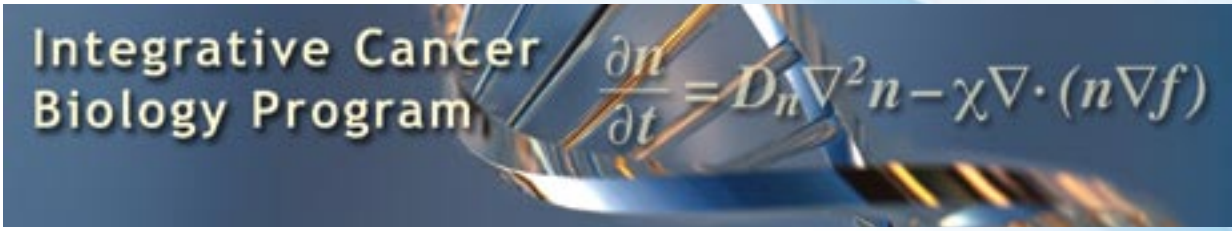
Although understanding cancer genetics is critically important to our ability to diagnose, treat, and prevent cancer in all of its forms, the biological complexity of cancer extends far beyond its genetic changes, into changes in protein function, structure, and metabolism that lead to cancer progression and metastasis. In order to develop a deeper understanding of these processes, NCI has undertaken several large multi-disciplinary team efforts to overcome obstacles to rapid progress, including developing best practices for biospecimen handling, standardizing proteomic technologies for valid biomarker discovery, defining the tumor microenvironment, and understanding cancer as a complex biological system.

OVERCOMING OBSTACLES TO UNDERSTANDING BASIC CANCER BIOLOGY

Office of Biorepositories and Biospecimen Research (OBBR): Almost all research into the molecular causes of cancer begins with tissue and DNA samples. In recent years, it has become clear to scientists that biorepositories with high quality biospecimens and data are needed to enable this work. NCI's OBBR is dedicated to providing leadership for biobanking activities that support all types of cancer research funded by the NCI. This is being done through a comprehensive approach to standard setting, biobanking science, and education with the aim of improving the quality of human biospecimens and biobanking operations nationally and internationally. The NCI Best Practices for Biospecimen Resources, issued in 2007, are a first attempt to standardize critical practices in biospecimen handling and banking in order to increase the meaningfulness and reproducibility of molecular data derived from experiments based on clinical samples from differing sources.

Clinical Proteomic Technologies for Cancer Initiative: The study of the structure and function of proteins and their interactions are major cornerstones of cancer research. Evidence suggests that measurements of even small amounts of cancer-specific proteins and peptides could be reliable indicators of cancer initiation and progression. However, studies that have applied protein measurement technology—including mass spectrometry and affinity-based detection methods—to detect these potential "biomarkers" have not been as successful as anticipated, largely because of significant challenges in the technologies themselves. In order to address this need, NCI launched the Clinical Proteomic Technologies Initiative for Cancer, a cross-institutional and multi-disciplinary team approach that networks multiple research laboratories in 2006 to permit large-scale, real-time exchange and application of existing and newly developed protein measurement technologies, biological resources, and data dissemination; refine, standardize, and optimize technologies, reagents, methods, and analysis platforms that will ensure reliable and reproducible separation, capture, identification, quantification, and validation of protein measurements from complex biological mixtures; evaluate new technological approaches to separate and recognize proteins of significance related to the molecular and cellular events that occur during the process of cancer development.

The Tumor Microenvironment Network (TMEN): Current cancer research reveals that tumors are not masses of cells developing independently, but function like organs composed of many interdependent cell types that contribute to tumor development and metastasis. Tumors and their surrounding cellular environment, collectively known as the stroma, evolve during tumor initiation and progression, and this interaction strongly affects the establishment and treatment of cancer. Evidence is emerging that critical stromal elements of the tumor are attractive targets for cancer prevention, because they primarily influence tumor cells in the early stages of cancer development. The TMEN program was established to expand the understanding of the role of the microenvironment in which a tumor originates and the critical role it plays in tumor initiation and progression. TMEN is a multi-disciplinary network that includes pathologists,



cancer biologists, cell biologists, oncologists, and experts in bioengineering and bioinformatics.

The Integrative Cancer Biology Program (ICBP): This effort focuses on the analysis of cancer as a complex biological system. The program brings clinical and basic cancer researchers together with researchers from mathematics, physics, information technology, imaging sciences, and computer science to work on key questions in cancer biology. The integration of experimental biology with mathematical modeling will provide new insights in the biology and new approaches to the management of cancer.

DEVELOPING THE ENABLING TECHNOLOGIES OF THE FUTURE

NCI is exploring, developing, and sharing significant new cutting-edge technologies that will continue the transformation of our understanding of cancer and how to address it, and help usher in the cancer clinical practice of tomorrow. These efforts include constructing the first of its kind informational infrastructure to link the diverse elements of the cancer community together in one united effort, exploring nanotechnology-based diagnosis and treatment possibilities, and finding new ways to image cancer at the subcellular level.

NEW TECHNOLOGIES FOR CANCER RESEARCH

Cancer Biomedical Informatics Grid (caBIG™): As we begin to better understand cancer at the molecular level and personalized medicine becomes a reality in cancer patient care, researchers and clinicians will require more rapid access to—and easier methods to analyze and utilize—the multiple types of information involved. Earlier systems to help translate the necessary data into better patient outcomes were disconnected or underperforming. caBIG™ serves as the cornerstone of NCI's biomedical informatics efforts to transform cancer research into a more collaborative, efficient, and effective endeavor. NCI launched caBIG™ to accelerate research discoveries and improve patient outcomes by linking researchers, physicians, and patients throughout the cancer community. The caBIG™ community has already developed and released a variety of bioinformatics tools and capabilities that span the entire continuum of clinical research, pathology and genomics, and more are under development. These tools, though developed for the cancer research effort, are already widely applicable beyond the cancer community.

caBIG™
cancer Biomedical Informatics Grid ™

NCI Alliance for Nanotechnology in Cancer

The NCI Alliance for Nanotechnology in Cancer: NCI is engaged in efforts to harness the power of nanotechnology—the field of research that deals with the engineering and creation of things from materials that are less than 100 nanometers (one-billionth of a meter) in size—to radically change the way we diagnose, treat, and prevent cancer. The NCI Alliance for Nanotechnology in Cancer is a comprehensive, systematized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. New nanotechnology approaches carry the potential to enable a new generation of targeted diagnostics, therapeutics, and preventives. Through the networked efforts of researchers at eight designated Centers of Cancer Nanotechnology Excellence, and the NCI's Nanotechnology Characterization Laboratory (NCL) at its NCI-Frederick facility, NCI is helping build the cancer medicine of the future using technology developed today.

TRANSLATING RESEARCH INTO CLINICAL PRACTICE: REDEFINING CLINICAL TRIALS

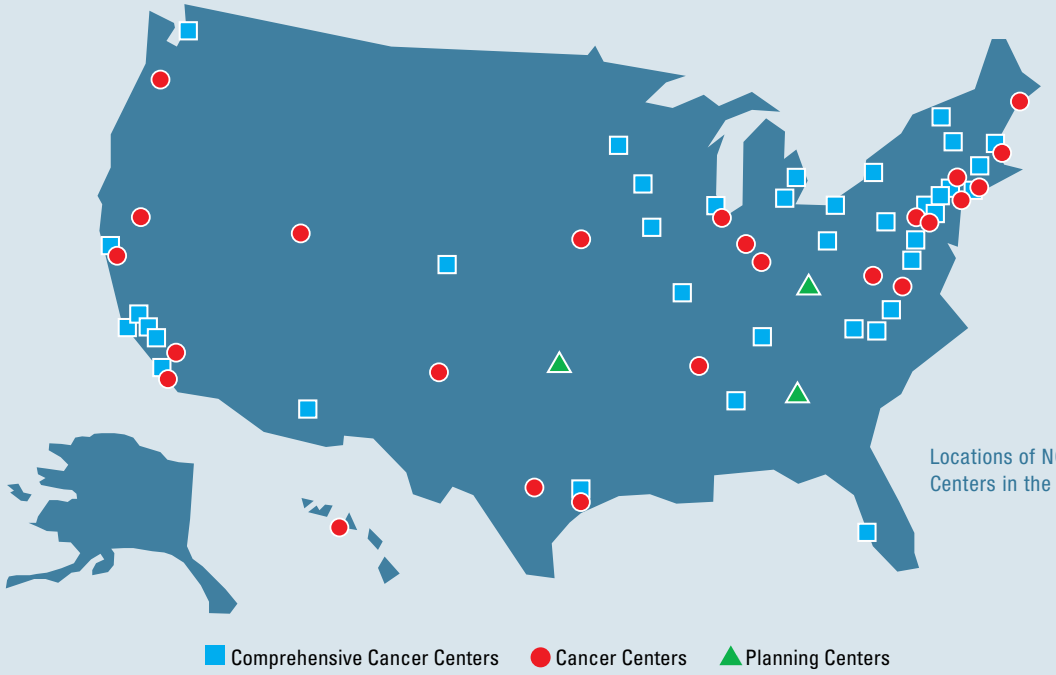
The enormous potential for more "personalized" cancer treatment, coupled with the complexity of evaluating new, highly specific therapeutic agents and diagnostic tests, demands a national clinical trials enterprise that integrates the knowledge, insights, and skills of multiple fields into a new kind of cross-disciplinary, scientifically-driven, cooperative research endeavor. Creating such an endeavor, endorsed by cancer centers across the U.S., will require greater integration of the successful, but functionally diverse, elements of the current clinical trials system supported by NCI.

To address this goal, the Clinical Trials Working Group (CTWG) of the National Cancer Advisory Board (NCAB) developed a detailed blueprint for "Restructuring the National Cancer Clinical Trials Enterprise." The strategy developed by the CTWG focuses on leveraging the unique strengths of the entire current NCI-supported clinical trials enterprise to bring about a system that is more effective, efficient, and facile.

This strategy specifically recognizes the role of NCI-designated Cancer Centers as a key institutional home for a large number of cancer clinical investigators, the strength of Specialized Programs of Research Excellence (SPOREs) in disease-oriented translational studies, the stable clinical trials infrastructure provided by the Cooperative Groups, and the ability of Community Clinical Oncology Programs (CCOPs) and other community oncologists to provide clinical trials in a local environment. The proposed restructuring preserves and strengthens all of the existing components of the NCI clinical trials system and enhances their ability to work together in fundamentally different ways.

The strategy developed by the CTWG addresses four important goals:

- Enhance coordination and cooperation by ensuring that comprehensive information on cancer clinical trials is readily available for all, that collaborative team science as well as individual achievements are rewarded, and that NCI clinical trials are effectively coordinated with federal regulatory systems.
- Enhance scientific quality and prioritization so that NCI supports the best-designed trials that address the most important questions, thereby leveraging significant scientific advances.
- Enhance standardization of tools and procedures for trial design, data capture, data sharing, and administrative functions to decrease effort and minimize duplication.
- Enhance operational efficiency by increasing the rate of patient accrual and reducing operational barriers so that trials can be conducted in a timely, cost-effective manner. In order to oversee implementation of the recommendations of the CTWG, an extramural advisory committee, the Clinical Trials Advisory Committee (CTAC), has been chartered. In addition, NCI has developed a coordinated, internal organizational structure to manage the entire clinical trials enterprise supported by the Institute. The Clinical Trials Operations Committee (CTOC) provides strategic oversight of the NCI's clinical trials enterprise while the Coordinating Center for Clinical Trials (CCCT) manages the implementation of the CTWG initiatives.



Locations of NCI-Designated Cancer Centers in the United States.

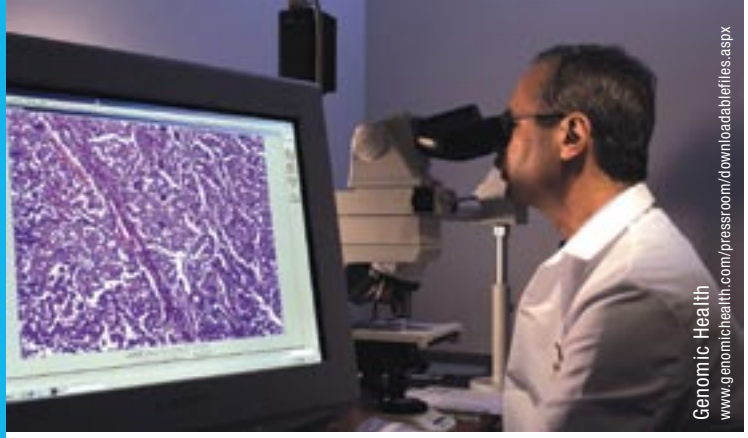
NCI-Designated Cancer Centers

The NCI's Cancer Centers Program is a critical component of the Institute's effort to provide infrastructure and manpower support for NCI-sponsored extramural science. The Cancer Centers Program supports 63 NCI-designated Cancer Centers nationwide that are actively engaged in transdisciplinary research to reduce cancer incidence, morbidity, and mortality. The NCI-designated Cancer Centers are a major source of discovery of the fundamental nature of cancer and serve as a key mechanism for translating those discoveries to patient care. These Centers, as well as other cancer centers throughout the country, deliver medical advances to patients and their families, educate healthcare professionals and the public, and reach out to underserved populations.

The NCI-designated Cancer Centers are directed by some of the finest leaders in the cancer community. The Cancer Center Directors have spent much of the last year examining the opportunities that exist to further the fields of cancer prevention, early detection, cancer treatment, and survivorship. They have identified areas for collaboration and areas of particular need. Their recommendations are outlined in the report, "Accelerating Successes Against Cancer" and serve as a valuable resource to the cancer research community and the NCI. Their recommendations have been incorporated into our overall strategic plan and are reflected in our need to expand certain areas of research.

Implementing the recommendations of the CTWG will require considerable effort by all stakeholders as well as financial investment on the part of NCI. This renewed commitment and the associated resources required are crucial for ensuring that the large, ongoing national investment in cancer clinical trials is effective and efficient in bringing effective new therapies to patients. By embracing this restructuring, NCI, cancer centers, and the oncology research community will be positioned to ensure that the advances in understanding the biological basis of cancer, generated by the past 40 years of research, are harnessed effectively to bring measurable, meaningful benefits to patients today and in the future.

Building on the plans outlined by the CTWG, NCI recently completed a two-year examination of early translational research and the opportunities and barriers that exist. The Translational Research Working Group (TRWG), a working group of the NCAB, was established to conduct a discussion with the broader cancer research community to develop recommendations about how NCI can best organize its investment to further translational research. The recommendations of this group were received by NCI in June, 2007, and the Institute is working on an implementation plan that integrates these activities with the infrastructure and support being created to support the CTWG.



A genomic health scientist reviews a slide to insure the tissue sample is suitable.

DISCOVERING AND DEVELOPING THE NEXT GENERATION OF EFFECTIVE AND EFFICIENT CANCER THERAPIES

NCI is not content to only understand the biology of cancer. NCI researchers are working tirelessly to find novel cancer treatments that do not harm healthy tissue, particularly for those types of cancer that are not being addressed by the private sector. We seek to find and evaluate such therapies, and then to develop collaborations with the private sector that will ensure that the therapies progress quickly to regulatory approval and clinical practice. To facilitate application, the NCI-designated Cancer Center Directors' report recommends enhanced collaborations among national organizations such as Centers for Disease Control and Prevention, Centers for Medicare and Medicaid Services, Health Resources and Services Administration, and Agency for Healthcare Research and Quality as key to successful dissemination of best practices for cancer care to reduce treatment heterogeneity or suboptimal care.

At the heart of NCI's internal efforts to find and develop new cancer drugs is the NCI's Developmental Therapeutics Program (DTP). In keeping with its goal to turn molecules into medicine for the public health, DTP, created by Congress in 1955 as the Cancer Chemotherapy National Service Center, serves as a vital resource in acquiring preclinical information and providing research materials, including vialed and plated compounds, tumor cells, animals, and bulk drugs for investigational new drug (IND)-directed studies. DTP has been involved in the discovery or development of more than 70 percent of the anticancer therapeutics on the market today. Successes include paclitaxel (Taxol®), one of the most widely prescribed anticancer drugs on the market, and bortezomib (Velcade®).

Paclitaxel, a natural product, was first harvested by researchers working under a joint U.S. Department of Agriculture-NCI grant. It was a DTP contractor who formulated the drug for use in clinical trials.

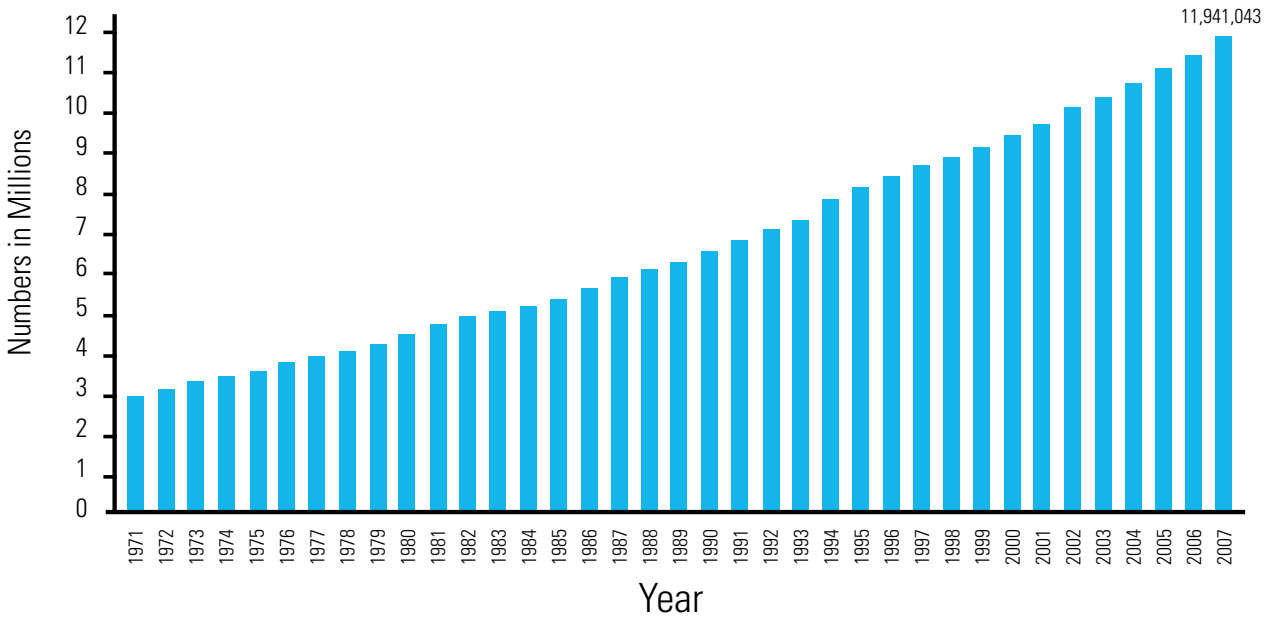
In cooperation with the commercial sponsor, bortezomib was screened and formulated by DTP. Approved by the FDA in 2003, it remains the first treatment in more than a decade to be approved for patients with multiple myeloma.

Although many academic and private-industry laboratories also are focused on drug discovery, NCI sees an opportunity to mediate novel academic-industry partnerships to overcome financial and technical barriers that may keep promising therapeutics from reaching patients. For example, a new direction for therapeutic drug development, made possible by the FDA Exploratory IND Guidance, is the Phase 0 clinical trial. These early studies are designed to determine if a drug shows favorable biodistribution, mechanisms of action and/or binding characteristics. These determinations are made in a limited number of patients using microdoses of the drug under investigation enabling "go, no-go" decisions earlier in the drug development process. NCI is developing these protocols, in many cases with industry partners, expediting the development and testing of promising therapeutics for cancer.

Clinical Trials: Optimizing Breast Cancer Treatment

The Trial Assigning IndividuaLized Options for Treatment (Rx), or TAILORx, was launched in May, 2006. Currently, the majority of women with early-stage breast cancer are advised to receive chemotherapy in addition to radiation and hormonal therapy, yet research has not demonstrated that chemotherapy benefits all of them equally. TAILORx seeks to incorporate a molecular profiling test into clinical decision making, and thus spare women unnecessary treatment if chemotherapy is not likely to be of substantial benefit. TAILORx is one of the first trials to examine a methodology for personalizing cancer treatment, and will ultimately enroll over 10,000 women at 900 sites in the United States and Canada. TAILORx is sponsored by the NCI, and is coordinated by the Eastern Cooperative Oncology Group (ECOG).

Estimated Number Cancer Survivors in the United States from 1971 to 2007



Data sources: NCI SEER November 2006 Submission, U.S. Estimated Prevalence counts were estimated by applying U.S. populations to SEER-9 and historical Connecticut Limited Duration Prevalence proportions. Populations from January 2004 were based on the average of the July 2003 and July 2004 population estimates from the U.S. Bureau of Census.

Approved Cancer Treatment Drugs Developed with DTP Involvement

2004	Erbitux® (NSC 632307)
2003	Velcade® (NSC 681239)
1998	Ontak® (NSC 697979)
1996	Gliadel® (NSC 714372) Topotecan (NSC 609699)
1995	All-t-retinoic acid (NSC 122758)
1992	Chorodeoxyadenosine (NSC 105014) Taxol® (NSC 125973) Teniposide (NSC 122819)
1991	Fludarabine Phosphate (NSC 312887) Pentostatin (NSC 218321)
1990	Hexamethylmelamine (NSC 13875) Levamisole (NSC 177023)
1989	Carboplatin (NSC 241240)
1988	Ifosfamide (NSC 109724)
1987	Mitoxantrone (NSC 301739)
1983	Etoposide (NSC 141540)
1982	Streptozotocin (NSC 85998)
1979	Daunorubicin (NSC 82151)
1978	cis-Platinum (NSC 119875)
1977	BCNU (NSC 409962)
1976	CCNU (NSC 9037)

1975	Dacarbazine (NSC 45388)
1974	Doxorubicin (NSC 123127) Mitomycin C (NSC 26980)
1973	Bleomycin (NSC 125066)
1970	FUDR (NSC 27640) Mithramycin (NSC 24559) o-p'-DDD (NSC 38721)
1969	Ara-C (NSC 63878) Procarbazine (NSC 77213)
1967	Hydroxyurea (NSC 32065)
1966	Pipobroman (NSC 25154) Thioguanine (NSC 752)
1964	Melphalan (NSC 8806) Actinomycin D (NSC 3053)
1963	Vincristine (NSC 67574)
1962	Fluorouracil (NSC 19893)
1961	Vinblastine (NSC 49842)
1959	Cyclophosphamide (NSC 26271) Thiotepa (NSC 6396)
1957	Chlorambucil (NSC 3088)

II. REACHING ALL COMMUNITIES TOUCHED BY CANCER.

Although the sheer complexity of cancer itself remains our most significant challenge, it is almost matched by the heterogeneity of the actual practice of cancer medicine across our nation. Part of NCI's mandate is to disseminate new knowledge and best practices, as well as clinical trial opportunities, to physicians and patients, regardless of location or social standing. It is a charge we take seriously, and we are making significant progress. In addition, we know that progress will continue to be made only if we make a concerted effort to identify, nurture, and train the next generation of talented researchers and clinicians.

THE NEED FOR RESEARCH ON ACCESS TO CANCER CARE

Although we are rapidly gaining new knowledge about cancer, we must get that new knowledge—the latest science—to patients. NCI maintains a network of 63 Cancer Centers, which are principally located at our country's premier research universities. Thirty-nine of those facilities, which conduct research and provide state-of-the-art cancer care, are designated as Comprehensive Cancer Centers. Yet, we are also aware that only approximately 15 percent of cancer patients are treated in these centers, with the great majority of the nation's cancer patients being treated in the communities where they live and work.

To address this significant access problem, NCI launched the NCI Community Cancer Centers Program (NCCCP) earlier this year, which is designed to study ways to bring new discoveries closer to the home of each cancer patient. The NCCCP, now in a three-year pilot phase, will encourage the collaboration of private-practice medical, surgical, and radiation oncologists and provide close links to NCI research and to the network of NCI-designated Cancer Centers. The pilot program will also study new and enhanced ways to assist, educate, and treat the needs of underserved populations—including elderly, rural, inner-city, and low-income patients—as well as racial and ethnic groups with unusually high cancer rates. Through this program, we will also learn how best to educate patients concerning cancer risk, healthier living, screening practices, clinical trial participation, survivorship, and end-of-life issues.

The NCCCP pilot will also study ways to bring early-phase clinical research to the community setting, along with emphasis on the standardized collection of biological specimens for research and the institution of electronic medical records. The NCCCP is designed to work in concert with other initiatives, in new settings, and with greater benefits for more patients.

"Mindful of our mission to conduct research in all areas of science—including the behavioral sciences, such as how best to provide patient education and access to optimal care—NCI is launching the pilot phase of the national Community Cancer Centers Program that, if fully implemented, will help bring state-of-the-art cancer care to patients in community hospitals across the United States."

Dr. John Niederhuber
Director, National Cancer Institute
Hearing Senate Subcommittee on
Labor-HHS-Education Appropriations
May 21, 2007


National Institutes of Health

ONGOING OUTREACH INITIATIVES

The Community Clinical Oncology Program (CCOP) network enables the participation by community physicians in national clinical trials studies. Participating in these trials makes it easier for community physicians to more quickly put successful regimens into practice. In fact, over its 23 years of operation, the CCOP, with more than 4,000 physicians participating at over 400 hospitals, has enrolled more than 200,000 people in treatment and prevention trials.

COMMUNITY-BASED INTERVENTIONS TO REDUCE CANCER HEALTH DISPARITIES

NCI's commitment to research that improves the quality of cancer care is a theme that runs through all of the Institute's research. Indeed, we still have much to learn about why some fare better with cancer than others, why some racial and ethnic groups have higher incidences of cancer than others, and how to assist those who may lack language capacity, mobility, or even the knowledge to navigate our healthcare system.

Up Close with a CCOP Patient

Sue Duyser was leading a busy life in Grand Rapids, Mich., running a pharmacy with her husband. Then she found a lump in her breast. Her doctors initially thought the lump was a cyst. "I was so busy, I let it go," says Ms. Duyser. Six months later, a friend who is a breast cancer survivor urged her to follow up with her doctors, and Ms. Duyser was found to have a late-stage cancer.

While extended family knew oncologists at the University of Texas M . D . Anderson Cancer Center, travel was not an option. Ms. Duyser is the primary caregiver for her husband, who has multiple sclerosis and uses a wheelchair. Networking through her community, she found the Grand Rapids Clinical Oncology Program, a CCOP site. There she found Dr. Marianne Lange, a dedicated physician willing to go the "extra mile" to get patients the best possible care. Ms. Duyser joined an NCI-sponsored clinical trial and though the treatment took many long and difficult months, Ms. Duyser knew she "was in good hands with the CCOP doctors" and was thankful to be able to be home with her husband, family, and friends. She is, today, a disease-free, 10-year breast cancer survivor.

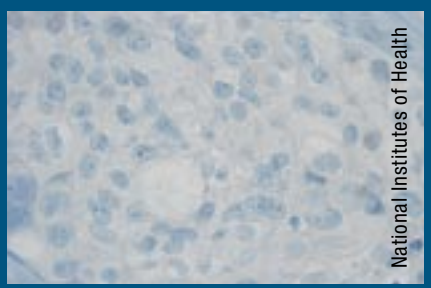
Two community-based programs of note—the Community Networks Program and the Patient Navigator Program—are further proof of that commitment to all of our citizens.

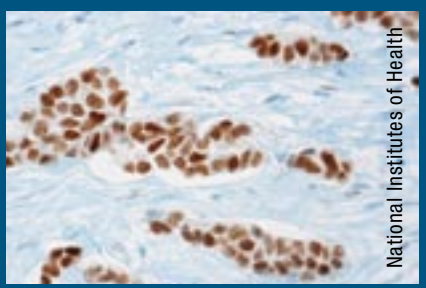
The Community Networks Program (CNP), which began in May, 2005 as a follow-up to our successful Special Population Networks program, works toward the reduction of disparities in cancer care, prevention, and survivorship through community-based participatory education, training, and research among racial and ethnic minorities and underserved populations. To date, NCI has awarded $95 million in 5-year grants to 25 institutions located in regions of the United States where the cancer burden is disproportionately high. Most sites have formed clinical partnerships that provide prevention services, including tobacco cessation, diet and exercise programs, and screening services for breast, prostate, colorectal, and cervical cancer. More than 640 partnerships with major cancer collaborators, such as the American Cancer Society, Susan G. Komen For the Cure Foundation, the National Urban League, state and local health departments, clinics, and hospitals, as well as regional offices of NCI's Cancer Information Service, help to build a strong and sustainable community-based infrastructure.

NCI's Patient Navigation Research Program (PNRP) focuses on developing and testing interventions to promote cancer awareness within communities and to help patients and their families manage cancer diagnoses and overcome common barriers to obtaining timely and appropriate cancer care and treatment. The primary participants for this research program are those experiencing cancer health disparities, encompassing racial/ethnic minorities, individuals with lower socioeconomic status, and residents of rural areas. PNRP captures valuable data for comprehensive evaluations of the effectiveness of its interventions in reducing cancer health disparities. For example, the program analyzes patient and navigator demographics and data on access to screening, diagnosis, and treament; quality of life; patient satisfaction; and cost effectiveness.

Health Disparities in Estrogen Receptor (ER) Negative Breast Cancer

About two-thirds of all breast cancer cells are ER-positive, meaning the tumors contain significant levels of receptors for the female hormone estrogen. The other third of breast cancers, ER-negative cancer, tend to grow more aggressively; they are more likely to metastasize, and are associated with a worse prognosis. Researchers suspect that the higher proportion of ER-negative tumors found in African American breast cancer patients, compared with white patients, may contribute to the higher breast cancer mortality rates seen in the African American population. Research to improve outcomes for patients with ER-negative breast cancer is an important strategy for addressing this health disparity. NCI is supporting identification and exploration of the basic biologic attributes of ER-negative breast cancer, including molecular mechanisms that can be targeted with prevention, early detection, and treatment interventions.





Two-thirds of breast cancer cells express the estrogen receptor (right), and one third—which tend to grow more aggressively—do not (left).

Cancer.gov en Español

More and more Americans are benefiting from advances in early detection and treatment of cancer. However, many Hispanics and Latinos in the United States have not heard this message and are unable to take full advantage of these options. By 2050, it is estimated that Latinos will make up a quarter of the U.S. population. National efforts to control cancer must include interventions and information directed at this group.

NCI's Spanish-language Web site **(http://www.cancer.gov/espanol)** strongly communicates the message that cancer can be prevented and treated, in addition to offering information on all aspects of the disease.

The site is tailored to meet the needs of Latinos who seek cancer information online. Rather than simply translating the English version of cancer.gov, the site was designed specifically for this audience. Cancer.gov en Español currently contains pages on different types of cancer, more than 100 peer-reviewed cancer treatment summaries for health professionals and patients, and a dictionary that includes 5,000 terms and definitions in both Spanish and English. NCI will continue to test and update the site to ensure that it meets the information needs of Spanish speakers.

Members of the NCI Minority Institute/Cancer Center Partnership Program

Life is different after cancer—emotionally and physically. Remembering that cancer is a process, and not an event, NCI leads the nation's research in cancer survivorship.

CANCER SURVIVORS

Life is different after cancer—emotionally and physically. Remembering that cancer is a process, and not an event, NCI leads the nation's research in cancer survivorship. The NCI-designated Cancer Center Directors' report identified survivorship as a major theme and recommended increased support to understanding all factors that affect a cancer patient's response to their disease and treatment. NCI researchers report that nearly one in four people diagnosed with cancer has participated in a support group. Furthermore, use of support groups varies considerably by cancer type, and few survivors receive physician referrals to such programs. Studies to show the value of such assistance may help clinicians recognize the importance of support groups for cancer patients.

BUILDING PARTNERSHIPS

The NCI Minority Institution/Cancer Center Partnership (MI/CCP) brings together NCI-designated Cancer Centers and Minority-Serving Institutions (MSI)—colleges and universities that are committed to the special encouragement of students from ethnic minority groups, including African Americans, Hispanic/Latino Americans, American Indians, Alaska Natives, and American Pacific Islanders. In addition to training, this collaboration focuses on reducing the disproportionate cancer incidence and mortality in minority populations. MSI and Cancer Center investigators are collaborating on more than 120 research projects. One example is the partnership between Nashville's Meharry Medical College—the nation's largest private, independent historically black institution dedicated solely to educating health professionals—and the Vanderbilt-Ingram

Cancer Center. Through their alliance, the two institutions are learning from each other and advancing student education, patient care, and research.

RESEARCH TRAINING AND CAREER DEVELOPMENT

As one way to continue the advancement of the entire cancer community, NCI is committed to training a future generation of American and international researchers dedicated to reducing cancer incidence, mortality, and suffering. Cancer researchers in the decades ahead will face a new landscape of challenges and opportunities. For this reason, NCI continually adapts its training programs to accommodate rapid developments in the frontiers of science and technology.

NCI devotes approximately four percent of its annual budget to institutional and individual research training and career development-related grants and programs. This investment provides support for scientists throughout their careers. There has been an emergence of new disciplines, changes in how cancer patients are treated, and an increase emphasis on communicating research-based information on cancer. NCI annually funds over 2,200 research training and career development awards. This number, however, represents only a portion of the training effort which is also supported in SPORE grants, the intramural research program and throughout the Research Project Grant (RPG) pool.

NCI uses these diverse training and development resources to provide support for individuals, from graduate students to established investigators, who need protected time away from administrative responsibilities to expand their research programs and mentor junior investigators. These investments will ensure a steady flow of well-trained investigators to focus on the challenges of fighting cancer and ultimately increase the diversity of the cancer research workforce.

A GLOBAL OBLIGATION

Cancer is not just a U.S. domestic issue. Each year more than 11 million people are diagnosed with cancer and more than 6 million die worldwide. That toll is greater than deaths from AIDS, tuberculosis, and malaria combined. NCI's international efforts are designed to foster research and build research capacity globally. NCI funds foreign contracts and grants, develops partnerships with other nations and organizations, and provides training opportunities for American scientists abroad and foreign scientists in the United States. NCI remains committed to supporting and expanding its international research efforts.

Dr. Grace Butler

Dr. Grace Butler does not just talk about cancer; she has lived it. Dr. Butler, a professor emeritus at the University of Houston, is a survivor of colorectal cancer who founded the non-profit organization called Hope Through Grace in 2002. The organization covers the cost of colon cancer screening for uninsured and underinsured populations and provides cancer awareness programs at shelters, churches, and higher education institutions, emphasizing underserved communities, including senior survivors of Hurricane Katrina who relocated to the Houston area.

Dr. Butler also freely gives her time to the service of all cancer patients. She is a member of both the NCI's Director's Consumer Liaison Group and the Consumer Advocates in Research and Related Activities (CARRA) program. Dr. Butler also attends important NCI meetings, such as the annual cancer health disparities summit, where she is an avid participant, sharing her passion for a healthcare system that reaches all cancer patients. In January 2007, President Bush visited the Clinical Center on the NIH campus in Bethesda, Md. He toured laboratories, met with patients, and conducted a roundtable discussion on the state of cancer research and treatment. Grace Butler was at that table too, representing those who have suffered with cancer and survived, determined to do something to help others.

Grace Butler, Ph.D., and President George W. Bush at NCI

Highlights of NCI's international efforts include:

Partnerships. The Middle East Cancer Consortium (MECC) includes Cyprus, Egypt, Israel, Jordan, the Palestinian Authority, and Turkey. Over the past decade, MECC has supported population-based cancer registries. NCI also acts as a sustaining partner of the Breast Health Global Initiative, which strives to develop, implement, and study guidelines to improve interventions for breast cancer in countries with limited resources.

Research. A global approach to research enables explorations of interactions between genes and specific environmental exposures found in diverse geographical settings. With the Chinese Center for Disease Control, NCI researchers have evaluated cancer risk associated with occupational exposure to benzene. The results of these studies were considered by the U.S. Environmental Protection Agency (EPA) in establishing a rule to limit the benzene content in gasoline, significantly reducing emissions of hazardous air pollutants in the United States. NCI-funded U.S. and Turkish researchers have studied malignant mesothelioma (MM), which accounts for 50 percent of all deaths in certain Turkish villages and has been linked with use of erionite, a carcinogenic mineral fiber. The researchers found that only some families suffer from a high incidence of the disease, because they possess a genetic predisposition that influences the development of MM. In addition to contributing to prevention and treatment for MM in Turkey, these studies also may improve prevention and treatment in the United States, where about 2,000 new cases of MM, primarily attributable to asbestos exposure, are diagnosed each year.

Cancer researchers in the decades ahead will face a new landscape of challenges and opportunities. For this reason, NCI continually adapts its training programs to accommodate rapid developments in the frontiers of science and technology.

Preparing The Next Generation

Dr. Sapna Syngal is an overachiever. She trained in internal medicine and gastrointestinal cancer, she focuses on the study of genetics, screening, and primary prevention of gastrointestinal tumors, primarily colorectal cancer. An assistant professor at the Harvard Medical School and a researcher at Dana-Farber Cancer Institute, Dr. Syngal sees patients, teaches postdoctoral students, and conducts cancer prevention research.

In 2000, Dr. Syngal received a Mentored Research Career Development Award. Her research to help reduce cancer incidence and mortality in individuals at high risk of colon cancer resulted in several other grants investigating genetic mutations in colorectal cancers.

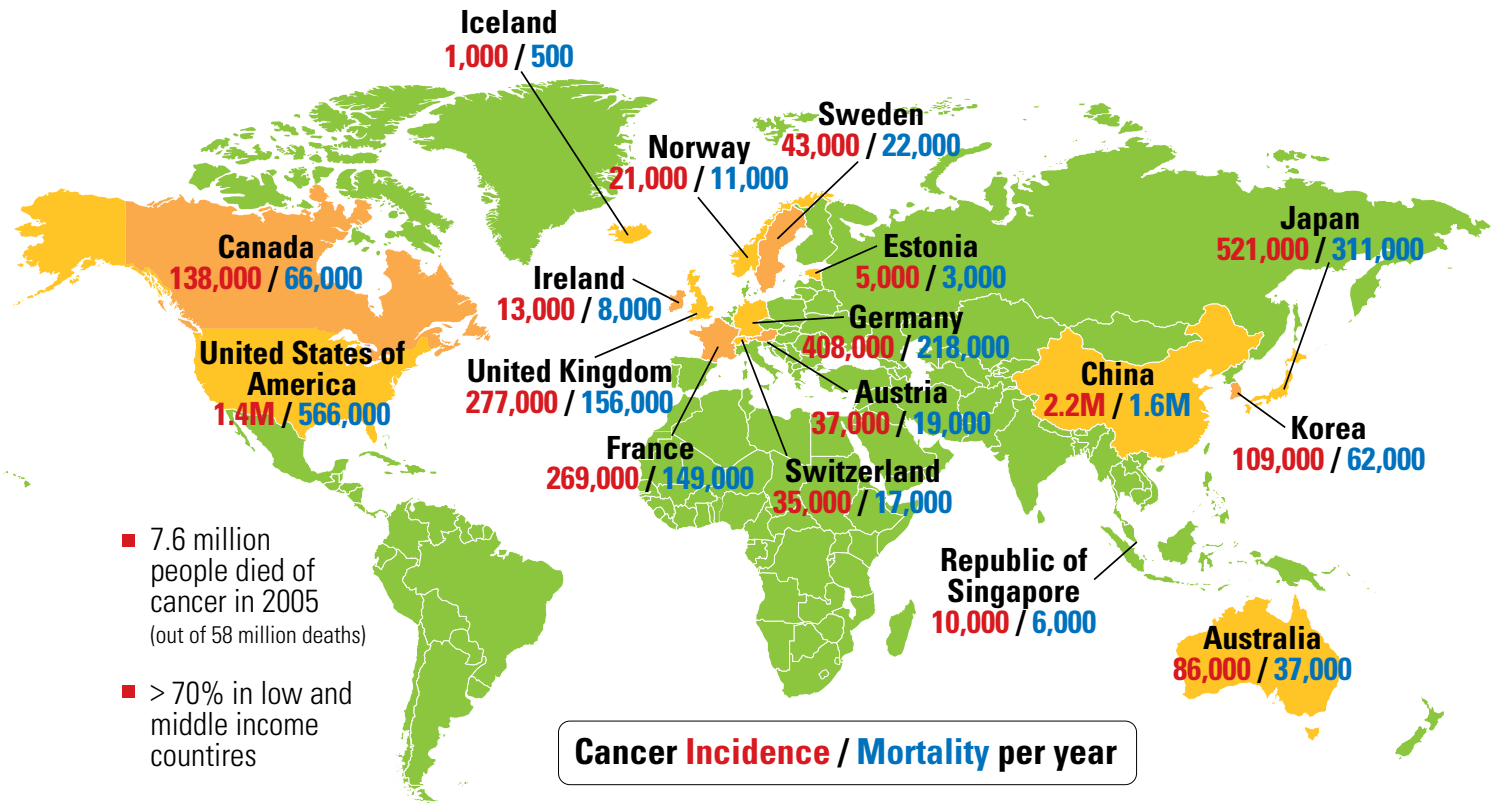
In 2005, Dr. Syngal won "protected time" through an NCI-supported Mid-Career Investigator Award, which freed her from administrative, teaching, and clinical duties so she could focus on mentoring young clinician investigators in patient-oriented research In 2005, Dr. Syngal worked with 14 postdoctoral clinicians, while continuing to further her research.

This outstanding clinical researcher is just one example of the people NCI and the NIH are honored to support through unique career development opportunities.

Sapna Syngal, M.D., M.P.H., is currently the Director of the Brigham and Women's Hospital/Dana-Farber Cancer Institute Familial Gastrointestinal Cancer Program.

Dana Farber Cancer Institute. Photo by Shawn Henry, used with permission

GLOBAL CANCER INCIDENCE AND MORTALITY



Source: International Agency for Research on Cancer, GLOBOCAN database

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Air pollution, a major contribution to cancer risk, in Shanghai, China

Cancer is not just a U.S. domestic issue. Each year more than 11 million people are diagnosed with cancer and more than 6 million die worldwide.

III. THE PROMISE OF PREVENTION AND EARLY DIAGNOSIS.

Despite many decades of investigation and progress made in early diagnosis and treatment, the exact causes of most cancers remain unknown. For most of the cancers we treat, there exists a mix of genetic changes and numerous environmental influences that challenge the development of simple prevention strategies. NCI's approach to cancer prevention is defined by the use of advanced tools and technologies—such as those employed in genomics, proteomics, and metabolomics—to dissect the molecular events associated with the molecular mechanisms and early signs of cancer development.

A new era of cancer prevention will require understanding genetic alterations, both those we are born with and those we accumulate throughout our lifetime, which can alter protein expression patterns and cellular function. These events will be further impacted by the need to understand environmental exposures and lifestyle factors. All of these layers point to the difficulty of finding effective, nontoxic preventive agents. Part of the solution involves identifying biomarkers of risk, as well as genome-wide association studies. For example, NCI's Early Detection Research Network is supporting researchers who are making important inroads in this area, including, promising preliminary work on an early detection assay for pancreatic cancer. Despite the complexity, NCI's extensive cancer prevention research program has generated some remarkable success stories, including the dramatic drop in smoking rates over the past two decades, as well as the approval of tamoxifen and raloxifene for the prevention of breast cancer. Thus, we continue to support research into lifestyle and environmental factors that influence cancer risk. These efforts include anti-obesity programs aimed at minorities conducted under the auspices of the Transdisciplinary Research on Energetics in Cancer (TREC) program as well as the development of new chemopreventive agents.

Prevention is, and will continue to be, an integral part of reducing cancer's burden. Identifying and quantifying an individual's risk of cancer and providing a tailored prevention strategy will be the cornerstones of a truly effective cancer prevention effort. NCI is actively working toward that goal.

UNDERSTANDING THE RISK OF DEVELOPING CANCER: THE NCI COHORT CONSORTIUM

The study of genetic and environmental risk factors for cancer has advanced considerably due to our investment in population studies. Researchers are using new genomic technologies, pooling resources, and sharing findings from large-scale studies, which are identifying gene variants that affect cancer risk, diagnosis, and prognosis. Underpinning the success of these studies is a long-term investment in the NCI Cohort Consortium. Comprised of 32 separate study groups including 4 million people, this cooperative, international endeavor collects biological specimens and associated risk factor data from a diverse group of populations. It provides a coordinated, interdisciplinary approach to tackling important scientific questions, while affording opportunities to quicken the pace of research and work across a collaborative network of investigators.

NEW PREVENTIVE THERAPIES: EARLY PREVENTION CLINICAL TRIALS CONSORTIA

To assess the cancer prevention properties of promising drugs and other agents, NCI is funding six chemoprevention research consortia. These groups will design and conduct Phase I and Phase II clinical trials, which determine safety and efficacy. The ultimate goal is to identify agents and strategies that can be tested in larger Phase III trials to determine whether a drug meets criteria for FDA approval. Consortia researchers will study the effects of these agents on molecular targets of cancer prevention, as well as on other biological events associated with cancer development, such as cell proliferation, cell death, the expression of growth factors, and the development of genes that cause cancer. Researchers will also correlate effects of the agents with clinical outcomes of trials, including survival and disease progression. The first 18 early-phase chemoprevention trials are now accruing patients and the consortia are developing 17 more trials.

TOBACCO AND TOBACCO-RELATED CANCERS

Tobacco use and exposure to tobacco smoke are the leading preventable causes of illness and death in the United States. Each year, more than 440,000 Americans die of tobacco-related disease, or one in every five deaths. Cigarette smoking is responsible for more than 30 percent of all cancer deaths annually in the United States. According to the World Health Organization, cutting tobacco consumption in half by the year 2020 would prevent approximately 180 million tobacco-related deaths around the globe.

NCI works with national and international partners, to understand the etiology of tobacco use, prevent initiation, develop and promote effective smoking cessation interventions, and improve survival of patients with tobacco-related cancers by developing earlier, more accurate diagnostic techniques and targeted therapies. For example, NCI-supported researchers investigate the biologic, genetic, and behavioral foundations of nicotine addiction and tobacco cessation; the causes of tobacco-related cancers; and the genetic and genomic factors affecting patient response to treatment and disease progression. NCI is committed to translating findings from this research into evidence-based prevention, cessation, and treatment interventions. NCI plans to broaden initiatives to examine the complex social, behavioral, environmental, biological, and genetic factors that influence tobacco use and tobacco-related cancers, including international consortia to address tobacco consumption in lower income nations

Obesity and Cancer

The Transdisciplinary Research on Energetics and Cancer (TREC) integrates the study of diet, weight, and physical activity and their effects on cancer by focusing on energy balance and energetics (the study of the flow and transformation of energy through living systems). NCI currently funds four research centers and one coordinating center as part of the TREC initiative. The TREC centers are fostering collaboration among transdisciplinary teams of scientists with the goal of accelerating progress toward reducing cancer incidence, morbidity, and mortality associated with obesity, low levels of physical activity, and poor diet. They also provide training opportunities for new and established scientists who can carry out integrative research on energetics and energy balance. The TREC initiative complements NCI's other energy balance research endeavors and efforts of the NIH Obesity Task Force.

and populations. The Transdisciplinary Tobacco Use Research Centers (TTURCs) seek to understand the determinants of tobacco use, nicotine addiction, and relapse, along with methods for preventing tobacco use across cultures.

Specialized Programs of Research Excellence (SPOREs) in lung, head and neck, pancreatic, and bladder cancers conduct translational research related to tobacco and tobacco-related cancers. For example, the University of Texas-M. D . Anderson Head and Neck Cancer SPORE is developing a tyrosine kinase inhibitor that shows antitumor activity in a tobacco carcinogen-based mouse model for both head and neck squamous cell carcinoma and non-small cell lung cancer.

TOBACCO CONTROL: PREVENTION AND CESSATION OF TOBACCO USE TO REDUCE DISEASE

The NCI-supported Cancer Intervention and Surveillance Modeling Network (CISNET) uses information on national trends in cigarette smoking to model how tobacco control interventions, screening modalities, treatments, and public policies may affect lung cancer incidence and mortality. Other studies help to identify tobacco control policies with the greatest potential for preventing tobacco use and second-hand (environmental) smoke exposure in populations disproportionately affected by tobacco use or tobacco company marketing. NCI also supports research to develop and disseminate culturally tailored, gender-specific, and language-appropriate tobacco prevention and cessation methods.

NCI supports research to improve people's ability to stop smoking. For example, researchers are learning how tobacco cessation treatments may be affected by genetic factors. Others studies are identifying gene variants associated with nicotine metabolism and risk of addiction that may provide new targets for cessation treatments. Still other researchers seek to understand and overcome barriers to quitting smoking, such as weight gain. NCI research also assesses the toxic and addictive properties of cigarettes and other tobacco products marketed as causing "reduced harm," and on smokeless tobacco.

NCI initiatives such as the Tobacco Research Network on Disparities (TReND), help to increase smoking cessation in underserved, low income populations. TReND includes the Low Socioeconomic Status (SES) Women and Girls Project to stimulate new research that will inform policies and programs to reduce tobacco use among this population.

TOBACCO-RELATED DISEASE: LUNG CANCER

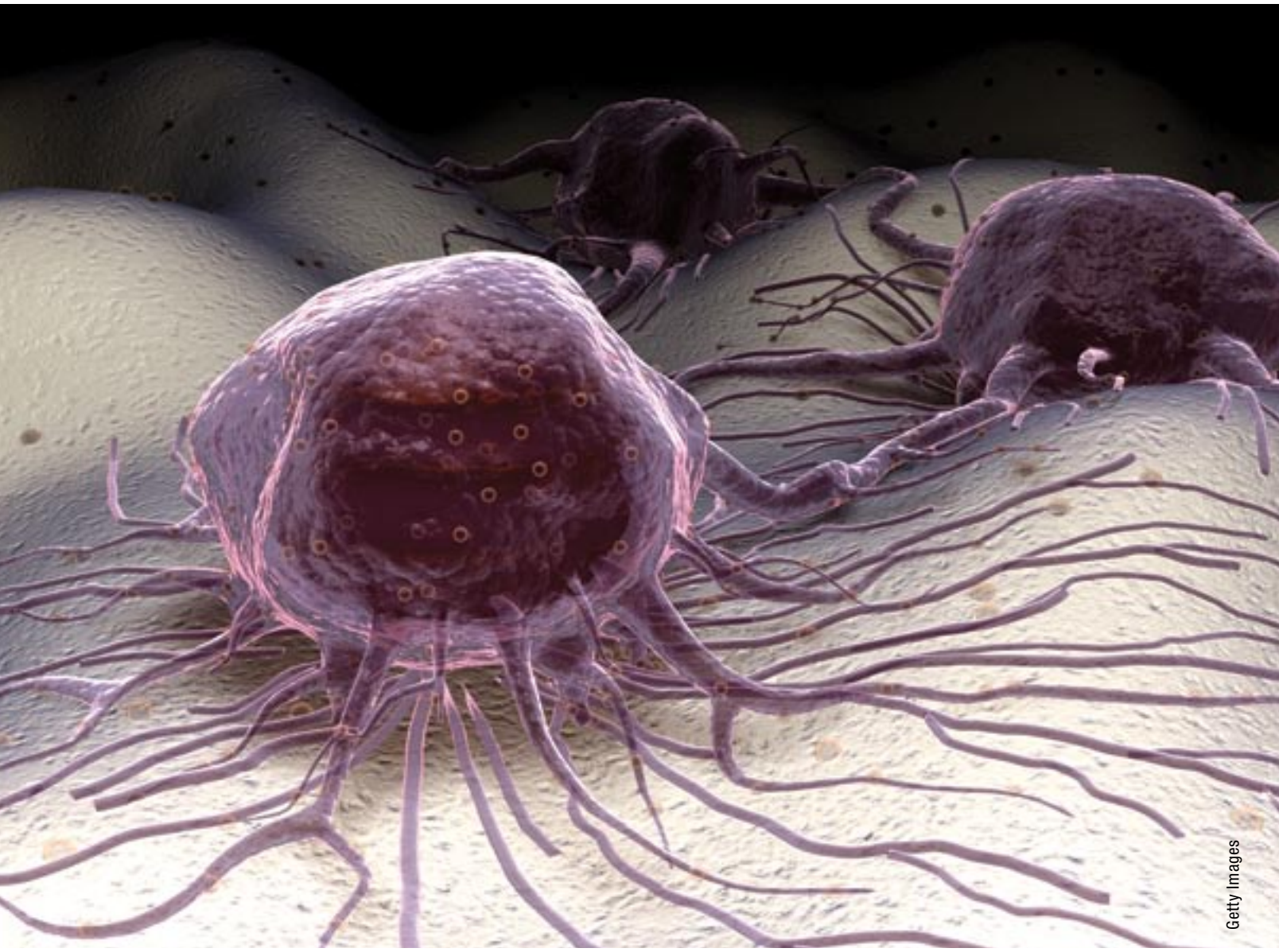
Examples of NCI research to lessen the burden of lung cancer and other tobacco-related diseases include the following:

Etiology: Population studies uncover the biologic, genetic, epidemiologic, environmental, social, and behavioral factors that interact with cigarette smoking and other tobacco exposures to cause cancer. NCI-supported case-control studies (which compare people who have a condition with people who do not) explore the genetics of lung cancer development, smoking persistence, and patient survival. Research on the link between the changes in the lung microenvironment caused by inflammation will help inform the process of cancer development and may inform our understanding of lung cancer in smokers, former smokers, and non-smokers.

Prevention: The Lung Cancer Biomarkers and Chemoprevention Consortium (LCBCC) conducts clinical trials and studies to identify blood-based biomarkers that can be used to assess response to chemoprevention agents.

Early Detection: The National Lung Screening Trial (NLST) and the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trials are following large

TReND
Tobacco Research Network on Disparities



A scanning electron microscopic image of a cancer cell and its processes on a cellular surface

groups of participants to compare the effectiveness of spiral-computed tomography (CT) against standard chest X-rays in reducing lung cancer mortality and to test the effectiveness of regular chest X-rays for lung cancer detection.

Treatment: NCI's lung cancer clinical trials are studying new treatment approaches to inhibit factors that stimulate growth of lung tumors. NCI's Imaging and Lung Cancer teams are planning research to advance the use of advanced imaging, such as FDG-PET (positron emission tomography), an imaging technique that produces a three-dimensional image of functional processes in the body, to detect a patient's response to a targeted therapy. Work to translate findings from this and other research into interventions to reduce the burden of tobacco-related cancers affords a potentially major opportunity to improve the health of people across the globe. For example, a drug called erlotinib (Tarceva®) is one of the "targeted drugs" that more specifically attack cancer cells, sparing normal cells. Erlotinib targets a protein called the epidermal growth factor receptor (EGFR). A protein that helps cells divide, EGFR is found at abnormally high levels on the surface of many types of cancer cells, including many cases of non-small cell lung cancer. By interfering with EGFR, erlotinib may keep tumors from growing. NCI is working to identify those patients for whom the drug, now approved by the FDA, offers the best outcome.

IV. NCI AT A GLANCE.

As the leader of the National Cancer Program, NCI is committed to enabling the connection between academia, the private sector, and other agencies within the federal government to drive progress for cancer patients and their families. By bringing unique resources to the table, NCI is able to leverage those with the expertise and support of the rest of the cancer community. Across its intramural and extramural efforts NCI supports basic, translational, clinical, and population research, technology development initiatives, research training and career development programs, research and management support infrastructure, and assessments activities.

INTRAMURAL RESEARCH PROGRAM

NCI is home to many of the world's leaders in cancer research. The NCI Intramural Research Program is allocated approximately 9 percent of NCI's research dollars and provides an unmatched environment that supports high-risk projects in basic, translational, and clinical research, along with epidemiological research studies that probe the incidence and distribution of cancer. A special strength of the intramural program is its ability to rapidly launch initiatives in response to emerging scientific needs and new opportunities.

NCI's intramural scientists, who in essence form the largest academic medicine research university in the world, have been tremendously successful largely thanks to their close access to the NIH Clinical Center, the world's largest hospital dedicated to clinical research. This state-of-the art facility provides an ideal environment for molecular epidemiology studies and genomic research to identify and validate genetic pathways and molecular targets that can lead to new approaches to cancer prevention, diagnosis, detection, and treatment. It is an ideal venue for testing drugs in their earliest phases of development. New approaches such as Phase 0 trials show great promise to shorten drug development time, improve drug safety, and drive down development cost.

EXTRAMURAL RESEARCH PROGRAM

Nearly 80 percent of NCI's budget funds extramural research activities—research taking place at institutions across the country and around the world. The Extramural Research Program supports cancer research in nearly 650 universities, hospitals, Cancer Centers, and other sites throughout the United

States and in more than 20 countries. The majority of NCI's extramural funding supports investigator-initiated Research Project Grants (RPGs). For Fiscal Year 2007, NCI invested more than $2.1 billion in support of over 5,200 RPGs. NCI's extramural budget also supports cancer control, investigator training, health disparities research, collaborations with the private sector, and other types of research and development activities.

Program experts within NCI guide and administer the investment in extramural biomedical research. They participate in the decision making process that identifies research goals and objectives, and recommend action for resource allocation. They also collaborate and maintain effective liaisons with scientists in their program area and monitor technologic, scientific, and policy developments to help identify future research opportunities and priorities. The extramural funding supports areas such as basic research into the workings and mechanism of cancer and its cells; research focused on cancer prevention, early intervention, symptom management, and supportive care; cancer diagnostic and therapeutic cancer interventions research; and research in surveillance, epidemiology, health services, behavioral sciences, and cancer survivorship.

NCI is leading an initiative to facilitate collaborations between intramural and extramural investigators by leveraging the NIH Clinical Center. At this national "clinical research laboratory" an important early-phase clinical trial for an aggressive form of a rare cancer, hereditary medullary thyroid carcinoma (MTC) was launched in July, 2007. The trial will determine whether the investigational agent vandetanib may be the first effective nonsurgical treatment in young patients with this cancer. But this trial is significant for another reason: It is the first being conducted at the NIH Clinical Center under the joint leadership of an NIH intramural clinical investigator and an extramural scientist. Dr. Frank Balis, from NCI's intramural research program, is the principal investigator (PI), while Dr. Samuel Wells,

Collaborations across Intramural and Extramural/ Public and Private Sectors

When she arrived at the Clinical Center at the National Institutes of Health, our patient couldn't even make a fist. Her hands, wrists, elbows, hands, and knees could scarcely bend. Her skin was cracking; her face was swollen and disfigured. 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, the nights spent in the hospital had come to greatly outnumber those she spent 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, decided to try 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, a year after her arrival at the Clinical Center, the patient's tests show no evidence of disease.

The drug utilized by Dr. Gutierrez was one that was developed, but never marketed, by a pharmaceutical company as a drug to prevent cancer. It was brought to the RAID program by an extramural investigator from Los Angeles, who developed it as a chemotherapeutic drug. Through its RAID program, NCI is able to take another look at agents that may not have fared well in a commercial environment, where the potential for profitability and market share are factors that must be considered. RAID offers the opportunity to further develop promising approaches for prevention, detection, and treatment.

Martin E. Gutierrez, M.D.
NCI Staff Clinician

The Clinical Center at the National Institutes of Health in Bethesda, Md., is the nation's largest hospital devoted to clinical research.

from Washington University in St. Louis and one of the world's foremost MTC experts, is the adjunct PI. Dr. Wells was involved in the discovery of a proto-oncogene, called RET, associated with the hereditary disorder multiple endocrine neoplasia (MEN). Patients with subtypes of MEN are at high risk of developing MTC and other endocrine tumors. Dr. Wells also helped to establish the efficacy of prophylactic thyroidectomy in children with RET mutations associated with these MEN subtypes.

After leading early-phase trials that demonstrated the activity of vandetanib in adults with MTC, Dr. Wells approached NCI about conducting a trial in children. It offered an ideal opportunity to pursue an intramural/extramural scientist-led trial. NCI worked with NIH leaders to make the arrangements allowing Dr. Wells to serve as a PI of a Clinical Center trial.

It is with rare cancers that the Clinical Center's value truly shines. Because NIH can recruit patients from around the country, trials performed at the Clinical Center are more likely to enroll enough patients with rare diseases to provide the statistical power needed to produce meaningful results and inform clinical care. Conducting the trial at the Clinical Center also allows investigators from other NIH institutes with expertise in endocrinopathies and MEN syndromes to participate. In addition to helping to write the trial protocol, these investigators provide clinical care to trial participants. And many patients in this trial—as well as members of their families, since this is a hereditary syndrome—will likely participate in additional studies, ensuring that the most scientific value from and clinical benefit for each patient during their treatment can be achieved.

The trial's Phase I/II design allows it to both determine the safest drug dose that can be given to pediatric patients and to evaluate its potential efficacy. The trial also involves biomarker and pharmacokinetic analyses, as well as analyses of tumor samples in the laboratory of NCI's Dr. Paul Meltzer to study whether there are genetic mutations associated with resistance to the agent.

This trial highlights a new vision of collaboration and partnership. It maximizes the potential of a single trial to provide as much data as possible so that the results can be quickly translated into patient benefit.

Patient rooms are in close proximity to cutting-edge laboratories doing related research.

It is with rare cancers that the Clinical Center's value truly shines. Because NIH can recruit patients from around the country, trials performed at the Clinical Center are more likely to enroll enough patients with rare diseases to provide the statistical power needed to produce meaningful results and inform clinical care.

V. THE 2009 BUDGET. (Professional Judgment Budget)

Successful outcomes from cancer research are the product of significant investments, not just of financial resources, but of time and professional dedication. Future success depends on sustained commitment to research so that we can truly deliver on the promise of personalized medicine. In order to fulfill this vital mission, the principles of the highest-quality scientific investigation, the development of enabling advanced technologies, and a pipeline of well-trained scientists and clinicians must be sustained.

OPPORTUNITIES

The National Cancer Institute is acting strategically to capture and leverage the opportunities before us, by building on previous research successes and wisely spending every dollar we receive. Emerging and expanding opportunities, reflected in this document, have been identified not in a vacuum, but by carefully listening to the entire oncology research community. NCI has the mandate to lead this effort, in addressing the fundamental issues that accompany the "preemption of cancer at every opportunity" and "assurance of the best outcomes for all": the dual core of the National Cancer Program.

The Impact of an Increased Budget: Recruitment and Funding of Scientists

NCI's ability to attract new, talented people into cancer research hinges on many factors, including continued financial investment. These young scientists are crucial for generating new ideas and translating them into scientific discoveries that benefit patients everywhere. An increase in scientific grant-supported research is absolutely necessary to encourage new scientists to bring their talents to cancer research rather than pursuing other well-funded areas, or to leave science all together.

A sign of this growing need can be seen in the fact that the average age of a first-time NIH grant recipient is now over 41—up from 34 in 1970. Grants receiving scores that in times of greater resources were competitive, now are not funded. Furthermore, the number of training awards for scientists has stayed level in recent years, even though the number of applications has continued to rise. This reality can be discouraging for seasoned scientists as well as trainees who, unable to obtain funding, are pursuing other careers at a time when we need them the most.

NCI recognizes the need to train individuals in new technologies, to foster team science, and to increase our research capacity. We are hopeful that the resources can be found to support training and career development.

Seizing the Opportunities at Hand

This plan—and the accompanying budget request—outline NCI's highest priorities for Fiscal Year 2009. With sufficient national investment:

1. Our Nation's position as a leader in biomedical research and development will remain strong.

2. We will enhance our ability to translate research findings to improve the quality of care and life for our increasing number of cancer survivors.

3. We can fully and rapidly utilize promising advances in cancer research, and ultimately realize the new possibilities for cancer prevention, early detection, and treatment for all.

The timing of these priorities coincides with a period when our country is experiencing an increase in new cancer cases, as the first wave of "baby boomers" begins to pass the age of 60 into the age bracket in which most cancers occur. Meanwhile, cancer will continue to affect people of all ages, and virtually every American will know someone affected by this disease. Our national investment in cancer research and treatment must be equal to the passion of our scientists and clinicians to ensure that the burden of cancer be lifted for all people.

These young scientists are crucial for generating new ideas and translating them into scientific discoveries that benefit patients everywhere.

This budget consists of two components: (1) the increase required to maintain our present level of operations or "current services", and (2) the increase required to initiate new and expand existing initiatives. The current services increase is the amount that will be required to sustain NCI programs, restore some of the funding cuts that have been implemented over the past several fiscal years, and provide for some minimal growth. Noncompeting Research Project Grants (RPGs) would be funded at committed levels, the success rate for competing RPGs would be maintained at its current rate, there would be a small growth in the number of Cancer Centers, and most other mechanisms would receive sufficient increases to cover cost of living adjustments based on the Biomedical Research and Development Price Index (BRDPI). This budget level also includes funds to make critically needed capital repairs and improvements at the NCI-Frederick Federally Funded Research and Development Center. The funds needed to initiate new and expand existing initiatives are add-ons to the current services level.

AT A GLANCE (dollars in thousands)

Fiscal Year 2008 Estimate	$4,925,740
Current Services Increase	334,638
Subtotal	5,260,378
Fiscal Year 2009 Additional Resources	
Increase Success Rate for Research Project Grants	65,000
Basic and Translational Science for Personalized Medicine	289,902
Linking Science and Technology	209,600
Reaching All Communities	72,100
Prevention and Early Detection	131,406
Subtotal	768,008
TOTAL, NCI	6,028,386

* Does not include the NCI contribution to the NIH Roadmap.

THE 2009 NCI PROFESSIONAL JUDGMENT BUDGET

(dollars in thousands)

Research Project Grants	FY 2007 Obligations	FY 2008 Estimate	Current Services Increase	FY 2009 Current Services	FY 2009 Additional Resources	Total FY 2009 Bypass	% Inc Over FY 2008 Estimate
Noncompeting	$1,597,609	$1,593,908	$101,303	$1,695,211	$0	$1,695,211	6.4%
Administrative Supplements	39,864	50,000	7,500	57,500		57,500	15.0%
Competing	440,193	495,950	98,050	594,000	306,000	900,000	81.5%
Subtotal	2,077,666	2,139,858	206,853	2,346,711	306,000	2,652,711	24.0%
SBIR/STTR	93,677	89,700	3,319	93,019	12,000	105,019	17.1%
Subtotal, RPG	2,171,343	2,229,558	210,172	2,439,730	318,000	2,757,730	23.7%
Research Centers & SPOREs							
Cancer Centers (P30/P20)	274,504	283,304	15,482	298,786	15,000	313,786	10.8%
SPORE (P50/P20)	159,478	160,478	5,938	166,416	29,200	195,616	21.9%
Other Specialized (U54/P50)	85,838	97,092	3,592	100,684	46,500	147,184	51.6%
Subtotal, Centers	519,820	540,874	25,012	565,886	90,700	656,586	21.4%
Other Research							
Research Careers	79,595	80,955	5,995	86,950	11,000	97,950	21.0%
Cancer Education	31,337	32,837	1,215	34,052	5,550	39,602	20.6%
Cooperative Clinical Research	238,403	245,603	9,087	254,690	28,250	282,940	15.2%
Minority Biomed. Res. Support	2,435	2,435	90	2,525		2,525	3.7%
Other	63,559	65,160	2,411	67,571	7,000	74,571	14.4%
Subtotal, Other Research	415,329	426,990	18,799	445,789	51,800	497,589	16.5%
Total Research Grants	3,106,492	3,197,422	253,983	3,451,405	460,500	3,911,905	22.3%
National Research Service Awards	68,223	69,933	3,588	73,521	10,000	83,521	19.4%
R & D Contracts	550,590	578,114	21,390	599,504	180,000	779,504	34.8%
SBIR/STTR	12,387	20,000	740	20,740	15,000	35,740	78.7%
Intramural Research	706,179	715,129	26,460	741,589	55,485	797,074	11.5%
Research Management & Support	353,211	357,222	13,217	370,439	20,023	390,462	9.3%
Construction (Capital Improvements)			6,000	6,000	24,000	30,000	
Buildings & Facilities	7,920	7,920	10,000	17,920	18,000	35,920	353.5%
TOTAL, NCI	4,792,615	4,925,740	334,638	5,260,378	768,008	6,028,386	22.4%

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