

The National Cancer Institute

The Nation's Investment in Cancer Research

*A Plan and Budget Proposal
for Fiscal Year 2002*

Prepared by the Director
National Cancer Institute

National Institutes of Health

What's Inside

Each year, as mandated by the National Cancer Act of 1971 (P.L. 92-218), the National Cancer Institute (NCI) prepares a plan for building on research successes, supporting the cancer research workforce with the technologies and resources it needs, and ensuring that research discoveries are applied to improve human health. This annual plan and budget proposal is provided directly to the President of the United States for formulating the budget request to Congress. This document also is used by NCI staff; the researcher community; professional organizations; advisory groups; cancer information, education, and advocacy organizations; and public and private policy makers. It is our hope that this document will inspire all who read it to join the fight against cancer. Here's what you will find inside:

OUR ROLE IN CANCER RESEARCH

NCI's goal is to stimulate and support scientific discovery and its application to achieve a future when all cancers are uncommon and easily treatable. Turn to [page 8](#) to learn about our approach to providing vision and leadership for accomplishing this goal.

HOW WE WORK

NCI conducts, coordinates, and funds cancer research and provides vision and leadership for the cancer research community in several ways. We describe our activities and core programs beginning on [page 14](#).

EXTRAORDINARY OPPORTUNITIES FOR INVESTMENT

New, intensive efforts and increased resources in six research areas offer the potential to yield profound insights that could lead to vast improvements in our ability to prevent, detect, diagnose, and treat cancer. Descriptions of these opportunities and our specific plans and resource requirements for addressing them begin on [page 63](#).

HOW IT ALL COMES TOGETHER

The efforts we describe in this plan and budget proposal all come together to make a difference for patients, families, and physicians struggling to find better answers to perplexing questions about cancer. See [page 100](#) to learn what this means for lung cancer, as an example.

PEOPLE'S STORIES

Dealing with cancer, and the threat of cancer, is an intensely personal journey filled with uncertainties, fears, and hopes. On [pages 22 and 61](#), two individuals share their stories.

FISCAL YEAR 2002 BUDGET REQUEST

A core budget will sustain our established research programs. Additional funding will allow us to continue building a research infrastructure for the future ("NCI's challenge") and to more rapidly expand on past discovery by taking advantage of "extraordinary opportunities." See [page 9](#) for a summary of our FY 2002 budget request.

HIGHLIGHTS OF PROGRESS

Every day, our nationwide programs for supporting cancer research yield new discoveries, new prevention and treatment approaches, and greater hope for people with cancer and those at risk. See [page 10](#) for highlights of recent scientific and technological progress.

NCI'S CHALLENGE: BUILDING OUR CAPACITY FOR FUTURE DISCOVERY

To ensure continued progress in the future, we need to focus on several aspects of our research infrastructure resources, technologies, organization, and personnel. For descriptions, plans, and funding requirements in each of these essential areas, go to [page 24](#).

PLANNING NATIONAL AGENDAS IN DISEASE-SPECIFIC RESEARCH

Progress Review Groups, a unique mechanism through which we work with the research and advocacy communities to chart the course of research for specific cancers, have become an integral component of our planning process. Learn more starting on [page 96](#).

ON THE CUTTING EDGE

NCI's Intramural Program will soon make tissue arrays on single slides available to researchers who need to study large numbers of tissue samples side by side. See [page 17](#).

SPOTLIGHTS ON RESEARCH

Exciting progress has been made in harnessing the immune system to prevent and treat cancer, in developing new detection tools, and in using new technologies to improve understanding of specific cancers. Turn to [pages 37, 76, and 82](#) to read special spotlights on these advances.

Director's Message

As the 21st century dawns, scientific discovery is occurring at a pace that would astound our forebears. Nearly every day some new advance, some new insight, brings us closer to answering one of the many questions that have long confounded scientists. Nowhere is the excitement generated by this new atmosphere of discovery more evident than in cancer research. The pace of discovery is continuing to accelerate, fueled by progress in three evolving areas:

The explosion of information on the fundamental nature of cancer. Over the past decade, scientists have gained stunning new insights into the fundamental mechanisms of the cancer cell. These remarkable discoveries hold promise for improving our ability to target prevention measures, to detect cancers early while they are most curable, and to develop treatments that are individually targeted for maximum results with the fewest side effects.

The development of new tools and approaches for conducting clinical research to test these insights in patients. Novel imaging technologies allow us to view activity at the molecular level. High-throughput tests that enable us to rapidly scan a person's genome for cancer-related abnormalities may soon allow us to more accurately assess individual risk or detect cancer earlier. Researchers and clinicians are now using workstations with high resolution medical image displays for real-time medical consultation from multiple locations around the world. Information management tools allow investigators to collect and analyze patient data in a more efficient fashion. All of these advances are enabling us to answer important clinical questions more rapidly, accurately, and effectively.

The growing sophistication in behavioral and population research that allows us to understand and address the burden of cancer. By identifying the forces and

factors that determine the burden of cancer – studying patterns of cancer, searching for causes, more fully comprehending the behaviors of individuals and communities, and understanding the impact of public health and medical systems – we are beginning to create the tools to effectively reduce that burden. We are gaining in our understanding of why some groups of Americans are disproportionately affected by cancer. We are using tools that give us clear and precise information on cancer trends among specific population groups and help us formulate hypotheses about why the trends occur. And we are better able to target our communications about cancer because we more fully understand our audiences and their needs.

Underlying these three areas of progress are several key changes in the overall research enterprise. First, we are witnessing and facilitating a fundamental change in the way scientific discovery is accomplished. Advances in our understanding of cancer at the molecular level, coupled with technologies drawn from the chemical, physical, and material sciences are enabling us to approach our research with a greater sense of predictability and precision. We are now able to move from empiric, fact-finding studies to “designed” research in which we identify a range of compelling options for prevention, detection, diagnosis, and treatment; verify their efficacy using models and electronic tools; and validate them through extensive testing and clinical trials. This fundamental change in how we approach research maximizes the effectiveness of all areas of scientific discovery, from broad-based science with potential to benefit all types of cancer to “disease-based” studies that focus on specific types of cancer.

Second, we are seeing an increasing amount of research that brings together and melds different

scientific perspectives and the tools of multiple disciplines. For example, by integrating the work of epidemiologists, geneticists, and population scientists, we hope to better understand the potential interplay among inherited susceptibility, lifestyle, and exposure to environmental pollutants and infectious agents in cancer causation. By combining the efforts of engineering technology and biomedical science, we have been able to devise highly sophisticated imaging tools for detecting, diagnosing, and even aiding in the treatment of cancer patients.

Third, our ability to do research on a large scale and with greater complexity has increased significantly. For instance, the development of common forms, terminology, and reporting requirements for use in cancer clinical trials is increasing the speed, efficiency, and accuracy of results reporting and analysis. We are also able to store and disseminate data on thousands of tumor tissue samples, making the data available to researchers around the world.

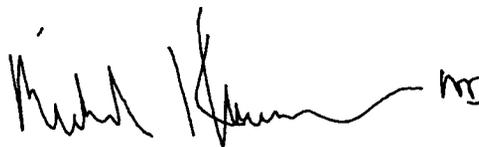
These areas of progress and the changes that underlie them are driving an evolution and rethinking of NCI's activities. Over the past few years, literally dozens of opportunities have been created – for example, the Phased Innovation Award, the Unconventional Innovation Program, and the Institute's functional imaging initiatives – to enable researchers to develop, access, and use new technologies. In addition, initiatives like the Cancer Genetics Network and the Early Detection Research Network bring together researcher communities and their collective resources, allowing them to ask questions on a larger scale. These new programs are accelerating the pace of discovery and speeding our efforts to unravel cancer's intricacies. As the depth of our knowledge of cancer grows, we will be able to bring the benefits of increasingly sophisticated scientific discovery to the American people more quickly.

Progress in our understanding of cancer and our ability to detect and treat it have led to a real and continuing decline in the cancer incidence and death rates. However, our excitement over impor-

tant scientific progress and the very real human gains that result is tempered by the knowledge that far too many Americans continue to suffer and die from cancer each day. Incidence of some cancers continues to rise. For example, the incidence of melanoma, a deadly skin cancer, has risen on average of 4 percent per year since 1973. Moreover, all groups of people are not benefiting equally from our advances against cancer. Rates of colon cancer, for instance, are declining overall, but not among African Americans. Too many Americans, for a host of reasons, lack access to high quality, cutting-edge cancer treatment and care. And, as more cancer patients are successfully treated, we recognize that we know far too little about the long-term needs of cancer survivors.

As we look forward to the next decade of progress, much remains to be done. This document, our plan and budget proposal for Fiscal Year 2002, describes in detail how we intend to proceed. Over the past five years, this document has come to be viewed as a national plan for cancer research and has been adopted by cancer researchers around the Nation. As such, it is no longer just a statement of the NCI's goals and priorities, but increasingly of the goals and priorities of the National Cancer Program.

The plans outlined in this document are ambitious – in some ways daunting. But the returns on our investment promise to be beyond price – no less than the prevention and cure of cancer. By continuing our investment in research and discovery, we will move ever closer to the long-awaited day when cancer is finally conquered.



Richard D. Klausner, M.D.
Director
National Cancer Institute

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Executive Summary

The National Cancer Institute's goal is to stimulate and support scientific discovery and its application to achieve a future when all cancers are uncommon and easily treated. NCI works toward this goal by providing vision to the Nation's cancer research effort and leadership for thousands of NCI-funded researchers across the United States and around the world. We:

- Conduct, coordinate, and support cutting-edge research and its application.
- Build upon past discoveries and promote creativity and innovation.
- Support development of, access to, and use of new technologies.
- Disseminate cancer information.
- Support training and career development for cancer researchers.
- Facilitate the movement of research findings into clinical practice.
- Maintain support mechanisms and collaborative environments to link scientists with their colleagues and with critical technological and information resources.
- Develop strategies to define, improve, measure, and monitor the quality of cancer prevention and care and reduce disparities in outcomes.

For all of our work, we depend on a superb workforce both inside and outside the Institute. We rely on the insight and advice of a broad spectrum of experts and advocates who serve on our standing advisory boards and committees and who assist with planning and assessment.

Our total Fiscal Year 2002 Budget Request is \$5,030,000,000. This represents an increase of \$1,524,928,000 over the Fiscal Year 2001 President's Budget. Of this increase, \$203,667,000

will be provided to continue NCI commitments into 2002 (Core Budget). An additional \$810,711,000 will be used for NCI's Challenge and \$510,550,000 will support Extraordinary Opportunities for Investment.

We will continue our work to sustain proven, productive research programs, build capacity for the future, and seize extraordinary scientific opportunities that build upon past discovery.

Sustain Proven, Productive Research Programs

Science cannot thrive without the resources that support an enterprise of discovery. NCI conducts, coordinates, and funds research through two key programs. Our Extramural Research Program supports individual basic, clinical, and population scientists, cancer centers, collaborative research teams, a comprehensive cancer control program, and training, education, and career development activities. Nearly three-quarters of our budget supports studies by thousands of investigators nationwide.

NCI also supports cancer research through our Intramural Research Program, which encompasses the work of over 400 principal investigators working in NCI laboratories and clinics. Approximately 16 percent of the Institute's budget is invested in this work. The Intramural Research Program complements ongoing research in universities and industry and has been involved in pivotal discoveries in cancer research, such as the first successful treatments for childhood leukemias, establishing the foundations for tumor vaccines, and identifying genetic causes of familial cancers.

Build Our Capacity for the Future (NCI's Challenge)

Major breakthroughs in cancer research depend on building and sustaining the strong research infrastructures and interdisciplinary collaborations that will enable us to apply rapidly evolving discoveries in cancer genetics, cancer biology, molecular-based technologies, imaging, and targeted therapeutic interventions. Our challenge is to provide the vision, creative environments, and diverse resources needed to ensure a smooth flow between advances in cancer research knowledge and their application in cancer prevention and treatment.

Investigator-Initiated Research

Investigator-initiated research – research conceived and conducted by scientists in laboratories and clinics across the country and at NCI – is the well-spring of scientific discovery. Our goal for Fiscal Year 2002 is to speed the rate of discovery and accelerate the application of those discoveries to the population by expanding and facilitating researchers' access to resources and new technologies. In understanding the basic processes of cancer and translating this research into clinical practice, we must link researchers with the resources and technologies they need, ensure collaboration, and encourage involvement of researchers across disciplines.

Centers, Networks, and Consortia

NCI will continue to create and sustain research infrastructures for collaboration, technology support and development, and access to resources that enable multiple scientific disciplines to address large problems in cancer that could not be solved by individual investigators. We will achieve this by expanding our nationwide infrastructure of cancer centers, centers of research excellence, networks, and consortia in ways that promote and facilitate complex scientific interactions and the sharing of information and resources.

National Clinical Trials Program

We will continue our efforts to ensure that the clinical trials program addresses the most important medical and scientific questions in cancer treatment and prevention quickly and effectively through

state-of-the-art clinical trials that are broadly accessible to cancer patients, populations at risk for cancer, and the physicians who care for them. As the research investment of the past decade has led to major advances in our understanding of tumor biology and potential molecular targets for cancer prevention and treatment, our capacity to apply and test these findings in clinical settings has not kept pace. The NCI will invest more resources in developing and testing new therapies and increasing access to and participation in clinical trials.

Studying Emerging Trends In Cancer

We will expand surveillance data systems, methods, communications, and training to improve capacity for monitoring progress in cancer control and for exploring potential causes of cancer nationally and among diverse populations. Recent changes in health care financing, information and computer technologies, and the social and cultural diversity of our country present new challenges and opportunities in surveillance research. In addition to traditional incidence and mortality data, we need data on patterns of care, patient-centered measures such as quality of life, and sociodemographic and economic population characteristics. New investments also are required to support and adopt new methodologic and informatics tools, including innovative approaches to modeling trends, more refined cancer maps, and information systems that will allow investigators to analyze individuals and potential environmental exposures by location.

Quality of Cancer Care

Our goal is to enhance the state of the science for defining, monitoring, and improving the quality of cancer care and inform Federal decision making on cancer care delivery, coverage, and regulation. NCI is launching research to improve the quality of cancer care by strengthening the information base for cancer care decision making. Researchers seek to better understand what constitutes *quality* cancer care, with an emphasis on the patient's perspective; identify geographic, racial/ethnic, and other disparities in who receives quality care; and strengthen the scientific basis for selecting appropriate interventions.

Reducing Cancer-Related Health Disparities

NCI is embracing the challenge of understanding the causes of health disparities in cancer and developing effective interventions to reduce them. Advances in biomedical science have contributed to increased longevity and improved quality of life for many Americans, but the burden of disease is not borne equally by all population groups in the United States. Plans call for increasing fundamental research into the social causes of health disparities, the psychosocial factors that mediate them, and the biologic pathways that can explain their impact. In addition, we will expand our cancer control intervention and population research on disparities, better define and monitor cancer-related health disparities, and strengthen training and education in this research area.

Informatics and Information Flow

NCI has taken on the challenge to create a cancer informatics infrastructure that enables cancer research by enhancing information and resource exchange among researchers, clinicians, and the public and reduces the barriers experienced by individuals seeking information about cancer prevention, diagnosis, and treatment. One of our first steps is to create a framework to increase the speed with which we carry out clinical trials by creating common forms, terminology, and reporting requirements. We will expand this infrastructure to enable integration among research initiatives of all types and improve information access for all user communities.

Training, Education, and Career Development

NCI will continue to expand its efforts to design and implement opportunities for scientists at all career levels to meet the challenge of building a stable, diverse cadre of basic, clinical, behavioral, and population scientists trained to work together effectively and use the most advanced technologies. We must more adequately prepare basic scientists, reverse the migration of physicians from research to practice, increase the numbers and stabilize the careers of population, behav-

ioral, and public health scientists, create a research workforce that is ethnically and racially diverse, and attract and integrate a wide array of technical and informatics disciplines into cancer research.

Seize Extraordinary Scientific Opportunities (Extraordinary Opportunities for Investment)

Six areas of extraordinary scientific opportunity in cancer research identified through formal input from cancer scientists, educators, advocates, and community leaders will be continued from Fiscal Year 2001 into 2002.

Genes and the Environment

Our goal in this area is to discover genetic, environmental, and lifestyle factors, and their interactions that define cancer risk and use this information to inform cancer prevention, early detection, and treatment strategies. We will achieve this goal through research on environmental risk factors, susceptibility genes, and their interactions; development of risk models to integrate genetic and environmental determinants of cancer; and clinical studies to address the clinical, behavioral, and societal issues associated with cancer susceptibility.

Cancer Imaging

To ensure continued exploration of the benefits of imaging technology in cancer, NCI will accelerate the discovery and development of imaging methods and use these new technologies to identify biological and molecular properties of precancerous and cancerous cells in order to predict clinical course and response to interventions. These developments will lead to a whole range of improved cancer prevention, diagnostic, and treatment options.

Defining the Signatures of Cancer Cells: Detection, Diagnosis, and Therapy

All cells have unique, identifiable “signatures”—a combination of active and inactive genes, and the proteins and other cellular products being manufactured by the cell. By reading cellular signatures accurately, we may be able to detect and diagnose

very early cancers before they invade nearby tissues. NCI's goal in this area of extraordinary opportunity is to generate a complete catalog of distinguishing molecular profiles of normal, precancerous, and cancer cells at all stages and in all tissues, and use the catalog to develop diagnostic techniques for the earliest detection of precancerous lesions and cancers; develop signature-based therapies; and identify subsets of patients with different prognoses to predict therapeutic response.

Molecular Targets of Prevention and Treatment

Many existing anti-cancer compounds inhibit the growth of cancer cells successfully, but they also affect healthy cells, causing short- and long-term toxic effects that can themselves endanger patients' health and quality of life. But advances in cancer biology, chemistry, and technology are providing the knowledge and tools to develop a whole new generation of cancer treatments and preventives that attack essential tumor cell processes with greatly reduced side effects. Our goal is to accelerate the discovery, development, and testing of prevention and treatment agents that target the molecular changes underlying various stages of cancer initiation and progression.

Research on Tobacco and Tobacco-Related Cancers

Over the past 30 years, we have learned much about the enormous burden tobacco use places on our Nation's public health, the cancer-causing agents in tobacco smoke, and the molecular changes that follow exposure to tobacco. Investigators also have learned a great deal about the psychosocial, biobehavioral, and biological determinants of tobacco use and addiction. NCI will build upon this knowledge base and devote increased resources to further understand the specific causes of tobacco use, addiction, and tobacco-related cancers and apply this knowledge to their prevention and treatment, particularly in high-risk individuals and groups.

Cancer Communications

The current communications revolution, particularly the power and potential of the Internet, is unprecedented in human history. At no other time has it been so easy for so many people to access such a vast wealth of information. But major gaps remain in our knowledge and understanding of how consumers use health information and how to improve access to it. Both the public and the physician community have a great need for timely, accurate cancer-related information on topics ranging from primary prevention to survivorship and end-of-life issues. NCI's goal is to understand and apply the most effective communications approaches to maximize access to and use of cancer information by the public, consumers, patients, survivors, and health professionals with a special focus on diverse populations.

The Nation's Investment in Cancer Research **NCI Budget Request for Fiscal Year 2002** (dollars in thousands)

Base of FY 2001 President's Budget	\$3,505,072
Core Increase	203,667
NCI's Challenge Increase	
Investigator-Initiated Research	124,561
Centers, Networks, and Consortia	93,500
National Clinical Trials Program	328,000
Studying Emerging Trends in Cancer	47,300
Quality of Cancer Care	21,500
Reducing Cancer-Related Health Disparities	50,600
Informatics and Information Flow	77,250
Training, Education, and Career Development	68,000
Subtotal Challenge	810,711
Extraordinary Opportunities Increase	
Genes and the Environment	68,250
Cancer Imaging	90,550
Defining the Signatures of Cancer Cells	110,750
Molecular Targets of Prevention and Treatment	146,500
Research on Tobacco and Tobacco-Related Cancers	67,000
Cancer Communications	27,500
Subtotal Opportunities	510,550
Total FY 2002 Budget Request	\$5,030,000

Our Role in Cancer Research

The National Cancer Institute's goal is to stimulate and support scientific discovery and its application to achieve a future when all cancers are uncommon and easily treated.

NCI works toward this goal by providing vision to the Nation and leadership for thousands of NCI-funded researchers across the United States and around the world and working to assure that the results of research are translated into reducing the burden of **all cancers for all people**. We:

- Conduct, coordinate, and support cutting-edge research and its application.
- Build upon past discoveries and promote creativity and innovation.
- Support development of, access to, and use of new technologies.
- Disseminate cancer information to our many communities.
- Support training and career development for cancer researchers.
- Facilitate the movement of research findings into clinical practice.
- Maintain support mechanisms and collaborative environments to link scientists with their colleagues and with critical technological and information resources.
- Develop strategies to define, improve measure, and monitor the quality of cancer prevention and care and reduce disparities in outcomes.

Our work is driven by careful planning and priority setting. This includes:

- *Defining and building a research infrastructure.* We give priority to developing the technological and personnel resources needed to support changing scientific and resource needs and the translation of new knowledge and emerging technologies into clinical practice.

- *Identifying extraordinary scientific opportunities.* We seek opportunities that promise to provide profound insights into cancer – those opportunities that hold greatest potential to lead to major improvements in our ability to prevent, control, detect, diagnose, and treat cancer.
- *Planning national agendas for disease-specific research.* We continually assess our portfolios and plan for the research needed to uncover the biological characteristics that are unique to specific forms of cancer.

Our success in these endeavors depends on:

- *A superb workforce both inside and outside the Institute.* The competence, hard work, and dedication of our researchers and clinicians and those who support their efforts each day drive our success in discovery and innovation.
- *Insight and advice from those who know and care most about cancer.* We look to representatives from a broad spectrum of scientific, medical, and advocacy communities in several ways:
 - Members of standing and special advisory groups assist us in planning for and evaluating cancer research from conceptual beginnings through clinical application.
 - Many people aid us in identifying, planning for, and implementing our “extraordinary opportunities for investment.”
 - People with diverse perspectives help us plan national agendas in disease-specific research through our Progress Review Groups.

NCI Budget Request for Fiscal Year 2002

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Budget Request		
			Core	Core and Challenge	Core, Challenge, and Extraordinary Opportunities
Research Project Grants (RPGs):					
Ongoing	\$1,103,744	\$1,245,664	\$1,401,840	\$1,401,840	\$1,401,840
New and Renewal	420,514	404,811	404,811	588,072	841,072
Subtotal RPGs	1,524,258	1,650,475	1,806,651	1,989,912	2,242,912
Small Business Innovation Research	67,046	71,337	73,121	86,121	100,121
Total RPGs	1,591,304	1,721,812	1,879,772	2,076,033	2,343,033
Intramural Research	511,786	532,002	545,302	584,802	586,802
Cancer Centers	173,609	182,216	186,771	239,771	269,771
Specialized Programs of Research Excellence	70,591	60,916	62,439	94,439	112,689
Clinical Trials Infrastructure:					
Cooperative Clinical Research	145,503	154,763	158,632	377,132	389,382
Community Clinical Oncology Program	62,173	69,232	70,963	138,963	170,963
Subtotal Clinical Trials	207,676	223,995	229,595	516,095	560,345
Training and Education Grants	121,564	133,971	138,446	202,546	207,046
Research Support Contracts	357,266	367,286	376,468	478,068	600,918
Cancer Control Operations	104,033	105,052	107,678	117,678	119,678
Research Management and Support	117,643	120,600	123,615	151,365	171,065
Other Grants	55,609	57,222	58,653	58,653	58,653
Total NCI	3,311,081	3,505,072	3,708,739	4,519,450	5,030,000
<i>Cancer Control included above</i>	365,837	375,367	383,668	541,768	681,018

Requested Increases for Fiscal Year 2002

	Core	Challenge	Extraordinary Opportunities	Total
Research Project Grants (RPGs):				
Ongoing	\$156,176			\$156,176
New and Renewal		\$183,261	\$253,000	436,261
Subtotal RPGs	156,176	183,261	253,000	592,437
Small Business Innovation Research	1,784	13,000	14,000	28,784
Total RPGs	157,960	196,261	267,000	621,221
Intramural Research	13,300	39,500	2,000	54,800
Cancer Centers	4,555	53,000	30,000	87,555
Specialized Programs of Research Excellence	1,523	32,000	18,250	51,773
Clinical Trials Infrastructure:				
Cooperative Clinical Research	3,869	218,500	12,250	234,619
Community Clinical Oncology Program	1,731	68,000	32,000	101,731
Subtotal Clinical Trials	5,600	286,500	44,250	336,350
Training and Education Grants	4,475	64,100	4,500	73,075
Research Support Contracts	9,182	101,600	122,850	233,632
Cancer Control Operations	2,626	10,000	2,000	14,626
Research Management and Support	3,015	27,750	19,700	50,465
Other Grants	1,431	0	0	1,431
Total Requested Increases	203,667	810,711	510,550	1,524,928

Highlights of Progress

Though cancer continues to be a real threat to human life and health, we are encouraged by the decline in overall incidence and mortality rates for cancer over the past few years. The rates of new cases and deaths for all cancers combined declined in the United States between 1990 and 1997.¹ Death rates for the four most common cancer sites – lung, colorectal, breast, and prostate – continue to drop, albeit slowly. And for the first time, between 1996 and 1997, the total number of cancer deaths did not rise, despite a growing and aging population.

That is the good news. The bad news is that death rates are still increasing for some forms of cancer including liver, non-Hodgkin's lymphoma, esophagus, multiple myeloma, and kidney cancers. The recent declines in the incidence of cancer stemming from the dramatic reductions in adult tobacco use may well be reversed if teen smoking continues to rise. Moreover, the overall number of Americans who develop cancer is expected to increase as our population ages and “baby boomers” enter the time of life when cancer is most common. An increase in the number of people with cancer will, in turn, place mounting pressure on our Nation's capacity to respond. With the expected growth and aging of the U.S. population, expenditures for cancer treatment are predicted to nearly double over the next decade, rising to just under \$100 billion. The costs of screening more people will add another five to ten percent to this bill. Keenly felt, but less easily calculated, are the productivity and contributions lost to society when people are afflicted with cancer.

Growing knowledge about the nature of cancer, newly developed tools and approaches for conducting clinical research, and increasingly sophisticated behavioral and population research techniques continue to provide ever improving options for preventing, detecting, diagnosing, and treating cancer. Still, the time required for discovery and breakthroughs can seem painstakingly slow. Each

endeavor takes a different course. Some things we can predict. Many we cannot. Some results come quickly while others take years. Learning what doesn't work is sometimes as important as learning what does. The following snapshot of recent progress in science and technology describes results from our past research investments and shows how these can fuel continued efforts in the areas described in this document.

Preventing and Controlling Cancer

- NCI is collaborating with two pharmaceutical companies to study the **effectiveness of the drug celecoxib in preventing several precancerous and cancerous conditions**. An earlier NCI study determined that celecoxib helped reduce the number of colon polyps in patients with familial adenomatous polyposis (FAP), a condition that is often a precursor to cancer. Based on this finding, the FDA approved celecoxib as an adjunct to usual care for patients with FAP. Through the National Clinical Trials Program, NCI and its partners hope to determine whether celecoxib is effective in preventing sporadic polyps, hereditary nonpolyposis colon cancer syndrome, Barrett's esophagus, bladder dysplasia, actinic keratoses of the skin, and the progression of FAP to colorectal cancer.
- The recently published **U.S. Public Health Service Report, *Treating Tobacco Use and Dependence: A Clinical Practice Guideline***, provides specific, evidence-based recommendations for brief and intensive tobacco cessation interventions and changes in the systems designed to promote tobacco use assessment and treatment. The guidelines outlined in the report, developed by a consortium of seven non-profit and government institutions including NCI, are based on an analysis of nearly 6,000 articles and abstracts published between 1975 and 1999.

¹ *Annual Report to the Nation on the Status of Cancer, 1973-1997*, prepared jointly by the National Cancer Institute, the American Cancer Society, the National Center for Health Statistics/Centers for Disease Control and Prevention, and the North American Association of Central Cancer Registries.

- Recently, **researchers have found evidence of nicotine dependence and withdrawal among young tobacco smokers before they become daily smokers.** NCI-supported researchers found that 63% of 7th-grade students who smoked one or more cigarettes a month reported experiencing one or more symptoms of nicotine dependence, such as cravings, withdrawal, and loss of control over the amount and duration of tobacco use. This and other recent studies indicate that – contrary to past assumptions – adolescents who have never smoked daily may encounter significant difficulty in trying to give up smoking, making it all the more important to develop new strategies to prevent young people from starting to smoke and to intervene early to help young smokers quit.
- NCI-supported researchers recently compared the outcomes of black and white patients with colon cancer enrolled in five clinical trials. They found, as have other analyses of NCI clinical trials, that **equal treatment yields equal outcome and that race is not a factor in cancer-specific survival when there is equal treatment.** Data from NCI’s Black-White Study of Cancer Survival showed that black and poor women with breast cancer were less likely to receive appropriate treatment after diagnosis. They also are more often diagnosed at a later stage of disease and are less likely to have a regular source of health care. Similar disparities in appropriate treatment have been demonstrated among various population groups with prostate, lung, and cervical cancers. NCI studies through the new NCI Challenge for Reducing Cancer-Related Health Disparities will focus on determining the reasons for the differences in care.

Detecting Cancer

- Preliminary research findings have shown that **testing for the human papillomavirus (HPV), the primary cause of 90 percent of cervical cancers, is a highly sensitive way to detect the underlying abnormalities that may progress to cervical cancer.** Investigators questioned whether HPV testing might help physicians and patients decide how to handle mildly abnormal PAP test results. Although most of these mild abnormalities will go away without treatment, physicians have had no way to distinguish the less serious abnormalities from those that will progress to precancerous conditions or cancer. Researchers concluded that the HPV test effectively detects abnormal lesions that need immediate attention. Through the Extraordinary Opportunity for Signatures of Cancer Cells, scientists will explore ways to improve the specificity of this test.
- Although early detection improves the likelihood that treatment will be successful, current non-invasive approaches for detecting small tumors have limited utility because they cannot distinguish small areas of abnormal cells from larger surrounding areas of normal tissue. Recently, however, scientists developed a new imaging method to more precisely view tumor cells, an important step toward non-invasive detection of small, and more treatable, tumors. The scientists injected tumor-bearing mice with a **unique imaging agent composed of near-infrared fluorescence imaging probes coupled with a novel substance that moves effectively into tumor cells.** When the agent was taken up by the tumors, cellular enzymes “activated” the agent causing it to fluoresce and allowing non-invasive detection. The agent was not activated in non-tumor cells. Using this technique, the investigators were able to image tumors smaller than three-tenths of a millimeter in diameter. Although this technique is still in the early stages of development, it illustrates the promise of new initiatives in the Extraordinary Opportunity for Cancer Imaging.

Treating Cancer

- Many cancer researchers have believed for some time that immunotoxins hold great promise for cancer treatment. The idea underlying this approach is elegantly simple: bioengineer small tumor-specific antibodies, link them to a powerful toxin, and directly target and deliver deadly poisons to tumor cells. Yet generating clinically active immunotoxins has proven to be a difficult challenge. A team of NCI scientists recently reported, however, that all patients included in a small trial on hairy cell leukemia, an unusual cancer of immune B cells, responded to a **recombinant immunotoxin called LMB-2**. One patient has been in complete remission for nearly two years, and the other patients had partial responses with significant reduction in the number of circulating malignant cells. None of the patients had responded to standard treatments. As many as 25 percent of hairy cell leukemia patients develop a resistance to conventional treatment, making this and other potential alternative treatments being tested through our Extraordinary Opportunity for Molecular Targets all the more promising.
- For many years, **hormone therapy (androgen deprivation)** was the only useful systemic treatment for advanced prostate cancers. It was never curative, however, and advanced cancers usually became resistant in one to two years. More recently, clinical researchers began to ask whether hormone therapy would be more beneficial if it were used before cancers ever become advanced. Patients with high-risk presentations of prostate cancer were randomized either to have early androgen deprivation (generally by injections every several months) along with initial radiation therapy or prostatectomy or not to receive androgen deprivation unless and until there was evidence of disease recurrence. All of the studies demonstrated a benefit to earlier hormone therapy. In one study, after a median of 6.8 years of follow-up, 85 percent of men in the adjuvant hormone arm were alive, compared to 65 percent in the group receiving hormone therapy only after their cancer recurred. A number of studies conducted through NCI's National Clinical Trials Program are now building on these results.
- The monoclonal antibody **Trastuzumab (commonly known as Herceptin™)** was the first targeted therapy for advanced breast cancer to receive FDA approval. Trastuzumab targets breast cancer cells with the protein Her-2, a molecule that straddles the cancer cell membrane, picking up signals outside the cell and relaying them inside to promote tumor growth. Blockage of the Her-2 receptor by the antibody reversed malignant transformation of cells. Human trials also confirmed the positive effects of Trastuzumab and demonstrated that this agent, when combined with chemotherapy, can prolong median survival by 24 percent in women whose tumors have high amounts of Her-2. Currently, NCI is sponsoring two major studies through the National Clinical Trials Program to test whether adding this agent to standard chemotherapy in earlier stages of breast cancer can enhance survival.
- **Bisphosphonates**, widely used to prevent osteoporosis, also have been shown to prevent bone breakdown due to malignancy. Because bone is the most common site of distant metastases in breast cancer, this disease has been a logical choice in which to test this approach. Several trials conducted with patients with bone metastases have shown that bisphosphonates can decrease the subsequent rate of fractures and other complications. NCI is now sponsoring two national trials to test whether bisphosphonates can prevent the development of bone metastases in breast cancer altogether. Findings from preliminary studies conducted in other countries have been equivocal regarding this effect, and larger studies are needed to provide a definitive answer.
- Development of the new drug **STI571** by Novartis Pharmaceuticals illustrates how NCI-funded molecular targets research can be translated into a powerful new cancer treatment. In nearly all patients with chronic myeloid leukemia (CML), leukemia cells express Bcr-Abl, an abnormal protein that alone is sufficient to cause CML. Because of this feature, CML

offered an ideal setting for testing the concept that an agent targeted against a tumor-specific abnormality can be an effective treatment. Researchers developing STI571 found that this **new drug targets leukemia cells** by selectively inhibiting cells that express the Bcr-Abl protein, making STI571 a promising candidate for treating CML and other Bcr-Abl positive leukemias. Initial results from a Phase I study demonstrated that virtually all patients treated with STI571 had a complete hematologic remission.

- **Thalidomide**, a drug that has been available only for limited use since it was discovered to cause birth defects in the children of pregnant women, **has shown effectiveness against Kaposi's sarcoma (KS), an AIDS-related cancer**. NCI researchers have shown in a Phase II clinical trial that thalidomide induced partial responses in 40 percent of the patients treated. The positive outcome of this trial warrants additional study of the drug, which inhibits angiogenesis. Thalidomide has also been shown, in early trials, to be active against multiple myeloma, a bone marrow cancer.
- Recent results from several clinical trials conducted to test the viability of **bone marrow transplants in combination with high-dose chemotherapy for treating metastatic breast cancer** exemplify how negative research findings are often as important as positive ones. In this case, the rigorous and costly regimens **did not prove superior to standard-dose chemotherapy**.

Understanding Cancer and its Causes

- NCI-supported scientists have identified a genetic mutation that may be responsible for **more than 11,000 of the 129,000 cases of colorectal cancer diagnosed annually in this country**. The TR-I(6A) defect, a mutant form of the Transforming Growth Factor Beta (TGF- β) receptor, may increase a person's risk for cancer. Comparing blood samples from cancer patients and healthy volunteers, scientists have observed that the TR-I(6A) mutation seems to occur more commonly in people with cancer than in healthy people. People who inherited a copy of

the mutation from both parents, and thus carried two mutant copies of the gene, had the most pronounced risk for developing cancer. The scientists suggest that this mutation may contribute to cancer development, particularly colon cancer, by hampering a cell's normal efforts to control its growth. This and other findings resulting from new efforts through the Genes and the Environment Extraordinary Opportunity may one day help physicians identify at-risk patients who should be monitored closely for early signs of disease.

- NCI researchers have found that **women who use combined estrogen-progestin replacement therapy have a greater risk for developing breast cancer than those who use estrogen alone**. Using 15 years of follow-up data from 46,000 women who participated in the Breast Cancer Detection Demonstration Project, a nationwide breast cancer screening program, scientists found that compared to non-users, the relative risk for breast cancer increased by eight percent per year for the estrogen-progestin therapy compared to one percent for estrogen therapy alone in women who had used hormones during the previous four years. There was no increase in risk among women who had stopped either therapy for more than four years. The increase in risk is still low for women taking both hormones, but this finding further complicates the decision women face about whether to take hormone replacement therapy.
- Using powerful new DNA microarray technology, a team of scientists recently determined that the **most common form of non-Hodgkins lymphoma (NHL) – diffuse large B-cell lymphoma (DLBCL) – is actually two distinct diseases**. The scientists discovered that DLBCL showed two distinct patterns of gene expression, suggesting that there are at least *two subtypes* of NHL, only one of which responds to current treatment. This finding underscores the importance of our Extraordinary Opportunity for Defining the Signatures of Cancer Cells as a path to more accurate diagnosis and targeted treatments. (For more information, see [page 82.](#))

How We Work

NCI conducts, coordinates, and funds cancer research and provides vision and leadership for the cancer research community by:

- Planning and prioritizing all aspects of the research we support.
- Conducting ongoing assessments to ensure a comprehensive and balanced research portfolio.
- Seeking advice regularly from our stakeholders.
- Supporting core extramural and intramural programs.
- Maintaining a strong infrastructure to support cancer research.

PLANNING AND PRIORITY SETTING

Research planning is an integral part of all NCI activities. It involves identifying needs and opportunities, setting priorities, and developing strategies for communicating and implementing decisions and recommendations. We set our funding priorities to ensure that we:

- Support the full range of research activities necessary to address the unanswered questions about cancer.
- Give attention to the spectrum of cancers and the various populations that experience them.
- Link all components of the cancer research enterprise through translational research.
- Identify new opportunities, gaps, and barriers to progress; create new programs; and improve existing ones.

ASSESSMENT

Assessment efforts ensure that our research portfolio is balanced and our support structure is strong. To implement recommendations arising from these assessments, we convene groups of outside scientists and NCI staff to redesign programs and develop new initiatives. We track implementation and regularly report on our progress.

Progress Reviews

We seek the advice of experts through Progress Review Groups (PRGs) to assess the scientific needs and opportunities that are critical to advancing research on specific forms of cancer. PRGs are composed of prominent members of the scientific, medical, and advocacy communities who work together to define, develop, and prioritize national research agendas. Go to planning.cancer.gov for more information.

Program Reviews

We use external reviews to guide us in strengthening our major research support programs. In the past few years, we have completed in-depth reviews of several programs including Cancer Centers, Cancer Control, Clinical Trials, Cancer Prevention, Developmental Therapeutics in Cancer, and Developmental Therapeutics in AIDS (deainfo.nci.nih.gov/advisory/bsa/bsa_program/pog_programfo.htm). In addition, implementation groups were formed and plans completed for advancing research in the areas of surveillance, tobacco, and nutrition (dccps.nci.nih.gov/DCCPS/SIG, dccps.nci.nih.gov/tcrb/TRIP, and dcp.nci.nih.gov/reports/nutrition/3intro.htm).

ADVISORY ACTIVITIES

To ensure the wise use of resources to meet the goals of the National Cancer Program, NCI actively seeks the expertise and perspective of a variety of advisory bodies both within and outside the Institute. (deainfo.nci.nih.gov/ADVISORY/boards.htm)

National Cancer Advisory Board

NCI's principal advisory body is the Presidentially appointed National Cancer Advisory Board (NCAB). Scientific experts and advocates on the NCAB advise NCI's Director on issues related to all aspects of the National Cancer Program and provide a second level of review for NCI grant applications.

President's Cancer Panel

The President's Cancer Panel, which consists of three persons appointed by the President, monitors the development and execution of National Cancer Program activities.

Board of Scientific Counselors

For advice on the progress, performance, and productivity of the Intramural Research Program, NCI leadership looks to the outside scientific experts and consumer advocates on the Board of Scientific Counselors. Members evaluate scientific programs through periodic site visits to intramural laboratories and advise NCI intramural divisions on future direction for their programs.

Board of Scientific Advisors

For advice on the progress and future direction of our Extramural Research Program, NCI leadership looks to the distinguished scientists and consumer advocates from outside NCI who serve on the Board of Scientific Advisors. Members evaluate Institute-awarded grants, cooperative agreements, and contracts and review ideas for new research solicitations to ensure that the concepts are meritorious and consistent with NCI's goals.

Advisory Committee to the Director

Members of the Advisory Committee to the Director make recommendations to the Director for the oversight and integration of various planning and advisory group activities. The Committee serves

as the official channel through which the findings and recommendations emerging from these groups are submitted. Members of this Committee include the chairs of all NCI standing advisory groups and the Institute's senior leadership.

NCI Executive Committee

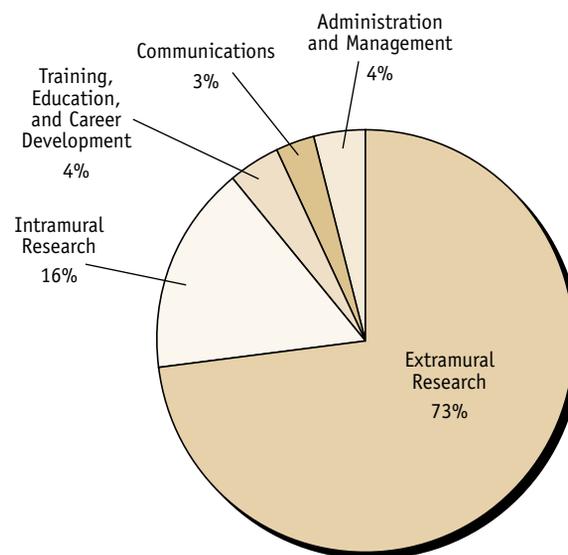
The NCI Executive Committee, which includes NCI division directors and other key advisors to the Director, meets regularly to make major policy and operating decisions for the Institute.

Director's Consumer Liaison Group

This all-consumer advocate advisory committee serves as a primary forum for discussing issues and concerns and exchanging viewpoints important to the broad development of NCI program and research priorities. The committee also helps develop and establish processes, mechanisms, and criteria for identifying appropriate consumer advocates to serve on NCI program and policy committees.

HOW WE SPEND OUR BUDGET

About 89% of the budget supports basic and clinical studies conducted through our core research programs. The remainder is used for preparing and developing researchers and clinicians at various stages in their careers, communicating cancer information to all who need it, and administration and management (nci.nih.gov/admin/fmb/index.html).



CORE RESEARCH PROGRAMS

NCI conducts, coordinates, and funds cancer research through two key programs: the Extramural Research Program (ERP), which links the NCI to investigators, teaching hospitals, and other sites throughout the country and the Intramural Research Program (IRP), which encompasses the work of over 400 principal investigators employed by NCI.

For information on each of NCI's divisions, go to cancer.gov/aboutnci.

Extramural Research Program

The ERP supports scientists; cancer centers; collaborative research teams; a comprehensive cancer control program; and training, education, and career development activities. Through the Divisions of Cancer Biology (DCB), Cancer Treatment and Diagnosis (DCTD), Cancer Prevention (DCP), and Cancer Control and Population Sciences (DCCPS), we support individual investigators and research teams from universities, private industry, and other Federal agencies.

DCB supports basic and applied research on cancer cell biology, including research on carcinogenesis; cancer immunology; and the role of biological, chemical, and physical agents in cancer initiation, promotion, and inhibition. DCTD supports research in five program areas: biomedical imaging, cancer diagnosis, cancer therapy evaluation, developmental therapeutics, and radiation research. Through DCP, we support an extensive research portfolio in cancer prevention including chemoprevention; nutritional sciences; genetic and infectious agents; and early detection through biomark-

er development, validation, and biometry. Through DCCPS, we conduct and support an integrated research program in cancer genetics; epidemiology; and behavioral, social, and surveillance research.

ERP program staff provide the essential scientific expertise and national focus needed to work with NCI-funded scientists. They synthesize the state of the science in their areas, identify priorities for new research directions, and foster collaborations among scientists. Program staff monitor the progress of extramural grants through contact with individual investigators and review of annual research progress reports. Results of these NCI-funded projects are communicated to the scientific community and the public through peer-reviewed scientific journals, scientific meetings, workshops, and symposia, and through our other cancer communication outlets, such as the Cancer Information Service, the Physician Data Query database, our press office, and our Web site (cancer.gov).

Research Project Grants (RPGs) are the main pool of funds expended by NCI for awards to extramural scientists. These funds foster the creativity of talented scientists by providing them with the support needed to pursue the best ideas that will yield progress against cancer.

RPGs are awarded to institutions for individual principal investigators while Program Project Grants go to groups of scientists involved in related research projects. In Fiscal Year 2001, NCI anticipates supporting 4,700 separate research grants, expending more than \$1.5 billion. More than 1,250 of these awards will be new or competing renewal projects. The individual investigator grant payline rose from the 15th percentile in Fiscal Year 1995 to the 22nd percentile in Fiscal Year 2000.

NCI also has special mechanisms to fund exceptionally innovative, exploratory, and developmental research activities, to allow investigators to embark on projects of unusual scientific potential, and to support research and development ideas that are likely to lead to a commercial product or service.

Intramural Research Program

The IRP is uniquely structured to address cancer research problems requiring long-term commitments and research activities not always conducive to extramural funding. The Program provides an environment conducive to cooperation between laboratory-based scientists and clinical investiga-

Research Project Grants (RPGs)

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
Ongoing	\$1,103,744	\$1,245,664	\$1,401,840
New	420,514	404,811	404,811
Subtotal	1,524,258	1,650,475	1,806,651
Small Business Innovation Research	67,046	71,337	73,121
TOTAL	1,591,304	1,721,812	1,879,772

Intramural Research

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
Basic	\$180,965	\$188,114	\$192,817
Clinical	131,965	137,178	140,607
Epidemiology & Genetics	52,973	55,065	56,442
NIH Central Services	145,883	151,645	155,436
TOTAL	511,786	532,002	545,302

tors to facilitate rapid translation of new basic research discoveries into early clinical trials. The IRP complements ongoing research in universities and industry and has been involved in pivotal discoveries in cancer research, such as the first successful treatments for childhood leukemias, establishing the foundations for tumor vaccines, and identifying genetic causes of familial cancers.

Within the IRP, the Division of Cancer Epidemiology and Genetics leads a national program of population-based studies to identify environmental and genetic determinants of cancer. The

Division of Basic Sciences (DBS) plans, directs, coordinates, and evaluates the Institute's intramural program in basic science relating to cellular, molecular, genetic, biochemical, and immunologic mechanisms relevant to understanding, diagnosing and treating cancer. The Division of Clinical Sciences provides the opportunity for patients from across the country to be treated through groundbreaking research protocols at NIH's Clinical Center. Because of its national stature and unique structure, the IRP is also a center for basic, clinical, and population-based oncology training for researchers from around the world. NCI plays a major role in fostering the education and careers of a growing number of nurses, doctors, and physician assistants.

KEY INFRASTRUCTURE COMPONENTS AND AREAS OF EMPHASIS

In addition to its core research funding programs, NCI provides support for research infrastructure and areas of emphasis including clinical research and cancer centers.

ON THE CUTTING EDGE

Developing Tissue Microarrays

Imagine how long it would take to determine if a new diagnostic test works by analyzing hundreds of tissue samples one by one. Cancer researchers nationwide may soon be able to dramatically shorten that step using a new tissue analysis technology. The new technology makes it possible to store hundreds of actual tissue samples on a single laboratory slide, in a "tissue microarray." Unlike traditional tissue analysis tools that allow scientists to examine only a few tissue samples at a time or other types of microarrays that contain only DNA, tissue microarrays permit scientists to examine hundreds of tumor samples at once.

Tissue microarrays may include samples from many different types of tumors for screening purposes or may contain tissues from various stages of a single kind of tumor for comparison studies. This new tech-

nology has astounding potential to accelerate research by hastening the process of identifying the unique characteristics ("molecular signatures") of cancer cells, information vital to continued advances in detection, diagnosis, and development of targeted cancer therapies.

The new Tissue Array Research Program (TARP) is a collaborative effort between the National Human Genome Research Institute and NCI. As one component of the Program, NCI will begin, in the Fall of 2000, to make tissue microarrays available to investigators across the country. The first to be offered will be screening microarrays with tissue samples from a variety of cancers such as colon, prostate, and breast.

For more information on TARP activities and services, go to cancer.gov/tarp.

Clinical Research

Clinical research is a cornerstone of the National Cancer Program. Every treatment we commonly use today, every widely recommended preventive measure, and every innovative detection strategy has been, at one time, tested in cancer patients or in people at risk for the disease. Participants in clinical research are often the unrecognized heroes of the fight against cancer who allow us to amass the body of information we are building upon every day. Trials provide participants access to cutting-edge interventions and provide researchers with information critical to continued advancement.

To test potential treatment advances more rapidly NCI maintains the Cooperative Group Clinical Trials program. The sheer number of different types of cancer and their biological complexity make the process of efficiently identifying and evaluating new treatments or other anti-cancer strategies extremely challenging. This national network consists of 12 consortia (Cooperative Groups) that collaborate regularly on clinical trials for a variety of common cancers, and they frequently work together when the clinical question requires such a large number of study participants that one group working alone would be unable to accrue enough people to conduct a meaningful study. Each year, 1,700 institutions throughout the United States and Canada and approximately 8,000 investigators in these institutions participate in these trials. This kind of cooperation makes it possible to centralize administration and data collection for trials taking place at a large number of sites around the world. Approximately 20,000 patients participate in Cooperative Group clinical trials each year, principally in large Phase III trials that help establish the state of the art for cancer therapy and prevention. Approximately 200 investigational agents or treatment strategies, ranging from new chemotherapy drugs and cancer vaccines to agents that prevent tumor blood vessel development, are currently being studied.

The Community Clinical Oncology Program (CCOP) is a network of 51 central offices in 32 states that provides the infrastructure to link more than 2,700 community cancer specialists and primary care physicians with clinical Cooperative Groups and cancer centers. This network enables individuals to participate in state-of-the-art clinical

Clinical Trials Infrastructure

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
TREATMENT:			
Clinical Cooperative Research	\$145,503	\$154,763	\$158,632
Community Clinical Oncology Program	8,078	8,275	8,482
Subtotal Treatment	153,581	163,038	167,114
PREVENTION:			
Community Clinical Oncology Program	54,095	60,957	62,481
TOTAL	207,676	223,995	229,595

research trials at over 350 community hospitals without the burden of traveling to a distant site. Eight minority-based CCOPs increase the participation of minority and underserved individuals in clinical trials research. Each year, over 700 patients enter clinical trials through these specialized CCOPs. In addition, CCOPs support scientific development and the implementation of ongoing cancer treatment, prevention, and control clinical trials among community Cooperative Group members and cancer centers.

NCI continues to take steps to address issues that threaten to compromise our ability to conduct clinical trials. These issues center around ongoing problems related to patient recruitment, changes in the health care system, insurance coverage, and recent public and media concerns about patient safety. To address these issues, NCI is:

- Developing ways to improve access and participation through the National Clinical Trials Program.
- Offering Established Investigator Awards to ensure that physicians have the time to conduct clinical trials (cancertraining.nci.nih.gov/research/clinical/k24.html).
- Working to assure insurance coverage for individuals participating in trials through agree-

ments with private insurers and other government agencies. (For extensive information about initiatives related to coverage for clinical trials, go to cancertrials.nci.nih.gov/understanding/indepth/insurance/index.html.)

- Working with patient advocate groups and professional societies, local communities, and non-profit organizations to increase understanding about clinical trials through education programs.
- Expanding initiatives to assure the protection of individuals participating in clinical research through increased oversight of studies, development of education programs for researchers, and grant support in the area of research ethics.

Initiatives involving other agencies and organizations are providing greater access and coverage for clinical trials. For example:

- NCI has established interagency agreements to secure coverage for Department of Defense and Veteran’s Administration health plan beneficiaries to participate in NCI-sponsored clinical trials.
- The United Health Care Corporation has agreed to provide coverage of patient care costs associated with cancer treatment trials conducted by the NCI-supported Cooperative Groups.
- A recent Presidential memorandum directs the Medicare program to reimburse providers for the cost of routine patient care in clinical trials and provides for additional actions to promote the participation of Medicare beneficiaries in clinical studies.
- Several states have enacted legislation designed to provide greater access and coverage for clinical trials.

Specific information about national and state initiatives is kept current and available in a legislation and insurance coverage section on NCI’s cancerTrials Web site. (cancertrials.nci.nih.gov/news/coverage/index.html)

Cancer Centers

Throughout the country, NCI has over 60 key partners in its efforts to speed the process of discovery and bring the benefits of cancer research directly to people. These research-oriented institutions, formally referred to as NCI-designated Cancer Centers in recognition of their scientific excel-

Cancer Centers/ SPOREs

(dollars in thousands)

	2000 Operating Budget	2001 President’s Budget	2002 Core Budget
Basic/Clinical/ Comprehensive	\$173,609	\$182,216	\$186,771
Specialized Programs of Research Excellence	70,591	60,916	62,439
TOTAL	244,200	243,132	249,210

lence, are hubs of cutting-edge research, high quality cancer care, and outreach and education for both health care professionals and the public.

Support for the cancer centers helps ensure a close association between state-of-the-art research and state-of-the-art clinical care within the institution. Moreover, it allows each center to develop key collaborations with industrial, community, and state health organizations, and to link the research capabilities and expertise of scientists within the institution to problems of cancer incidence and mortality in their communities and regions.

There are three types of centers: **Cancer Centers** have specific research foci, such as epidemiologic or basic research; **Clinical Cancer Centers** concentrate on research activities in clinical oncology; and **Comprehensive Cancer Centers** demonstrate both significant scientific strength in laboratory, clinical, and population studies and strong interdisciplinary collaboration. Comprehensive Cancer Centers also must have in place effective cancer information, education, and outreach activities for the regions and communities they serve.

Traditionally, cancer centers have had broad scientific bases, and most have been developed within a single institution. Changes in the program, however, are enabling the planning of new consortia of institutions, often linking free-standing clinical and academic centers with community hospitals to form networks. In addition, more focused scientific concepts are being developed for cancer centers. For example, some centers are focusing on population sciences and others are concentrating on translational research opportunities within a specific scientific discipline, such as immunology. Go to cancer.gov/cancercenters for more information.

Specialized Programs of Research Excellence

To move discoveries more rapidly from the laboratory to patient and population settings, NCI created Specialized Programs of Research Excellence (SPOREs). Through the SPORE mechanism, we can award sizable amounts of flexible funding to enable teams of researchers to address emerging scientific opportunities in disease-specific research. Since 1992, NCI has supported SPOREs in breast, prostate, lung, gastrointestinal, and ovarian cancers. Plans are underway to support lymphoma, head and neck, genitourinary tract, brain, and skin cancer SPOREs over the next several years. The SPORE concept is being broadened beyond a disease-specific focus to include support of Centers of Research Excellence – interdisciplinary research teams focused on a disease modality, biologic process, or scientific area of particular interest. These include the Tobacco Use Research Centers and Interdisciplinary Research Teams for Molecular Target Assessment.

Cancer Control

Cancer control encompasses a full spectrum of research in the behavioral, social, epidemiologic, and population sciences aimed at creating or enhancing interventions that, by themselves or in combination with biomedical approaches, reduce cancer risk, incidence, morbidity, and mortality, and improve quality of life. For example, a cancer control study might investigate the use of a medical

intervention, such as a nicotine patch, in combination with a behavioral intervention, such as a counseling program to help smokers quit. Interventions may be directed at patients, physicians, and/or other health care providers. Cancer control research seeks to improve interventions across the human lifespan and over the entire cancer continuum, and to move research findings into clinical and public health practice. The foundation of cancer control research is epidemiology. Surveillance and outcomes research are the fundamental mechanisms for assessing progress.

NCI maintains a firm commitment to cancer control research through its Divisions of Cancer Control and Population Sciences and Cancer Epidemiology and Genetics. Our wide-ranging efforts include research in epidemiology and genetics, tobacco, tailored communications, and theoretical models for studies of human behavior and behavior change.

AIDS Research

Malignancies occur in more than 30 percent of patients living with AIDS and contribute greatly to health consequences and death. Research into the fundamental biology of HIV and AIDS, AIDS treatment, and particularly AIDS-related malignancies takes place throughout NCI. The IRP is an internationally recognized center for research in HIV and AIDS, housing the HIV Drug Resistance Program, the HIV and Malignancies Branch, and the NIH Vaccine Research Center, a joint project with the National Institute of Allergy and Infectious Diseases (rex.nci.nih.gov/RESEARCH/basic/dbslabs.htm). The ERP also has been a vital and innovative force in this area of research. Among its programs are the AIDS Malignancy Consortium, the AIDS Malignancy Bank, the AIDS Oncology Clinical Scientist Training Program, and an annual international forum on AIDS malignancies. NCI, in coordination with other NIH Institutes and the NIH Office of AIDS Research, continues its commitment to AIDS research and is working to ensure that NCI-supported AIDS and AIDS-related research is integrated with national AIDS strategies. Go to ctep.info.nih.gov/AIDSOncoResources for more information.

Cancer Control*

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
Grants	\$152,256	\$163,777	\$166,789
Contracts	109,548	106,538	109,201
Cancer Control Operations	104,033	105,052	107,678
TOTAL	365,837	375,367	383,668

* Cancer Control grant and contract funds are distributed among appropriate extramural mechanisms.

Training and Education

NCI is implementing a long-range plan for extramural training, education, and career development designed to prepare and sustain the national cadre of trained cancer researchers critical to current and future endeavors. This plan focuses on attracting young scientists into cancer research, providing stability and protected research time for researchers in disciplines critical to translational research, creating more opportunities for scientists from underserved ethnic and minority groups, and encouraging research program diversification. In pursuit of these objectives, NCI has implemented a number of new training and career development programs in basic, clinical, population, and diversified sciences as well as for ethnic and minority groups who are underrepresented in the research workforce.

Training and Education

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
National Research Service Awards	\$58,654	\$62,445	\$64,006
Research Career Program	40,424	45,525	46,663
Cancer Education Program	18,886	21,978	22,527
Minority Biomedical Research Support	3,600	4,023	5,250
TOTAL	121,564	133,971	138,446

Other Research Support

In addition to its many types of grants and awards, NCI employs a variety of other research support mechanisms. These mechanisms include:

- Contracts to provide support for research, information dissemination, and management
- Conference grants to fund meetings, conferences, and workshops

- Resource-related awards to foster partnerships and meet needs for shared resources such as specialized databases and instruments
- Scientific evaluation awards to support the scientific review of grant and contract proposals
- Construction grants and contracts to provide partial support for modernizing or developing cancer research facilities throughout the Nation

NCI also sustains, guides, and monitors the extramural and intramural activities of the Institute through its research management and support activities. These activities include overall scientific program direction and administration by grant and contract science managers and finance, human resources, legislation, science program direction and assessment, and technology transfer staff. The review and oversight activities of the National Cancer Advisory Board and President's Cancer Panel are also included. This part of the budget also supports a share of central NIH facilities and operations, and extramural program staff salaries. (Intramural staff salaries and intramural facilities maintenance are included under the intramural research budget.)

Other Research Support

(dollars in thousands)

	2000 Operating Budget	2001 President's Budget	2002 Core Budget
Research Support Contracts	\$357,266	\$367,286	\$376,468
Scientific Evaluation Grants	4,981	6,342	6,501
Research Resource Grants	45,905	46,263	47,420
Construction Conference Grants	3,500	3,000	3,075
Conference Grants	1,223	1,617	1,657
Research Management & Support	117,643	120,600	123,615
TOTAL	530,518	545,108	558,736

Adult and Pediatric Brain Tumors

I was diagnosed with a brain tumor six months ago. As frightening as it can be to have a brain tumor, I know I'm lucky that mine is one of the less aggressive types.

There are more than 100 types of central nervous system (CNS) tumors. Some are highly aggressive and rapidly fatal, while others grow slowly and may be present for years before the patient feels any effect. People with very slow-growing tumors may live with them for decades and eventually die of an unrelated cause.

CNS tumors differ from other solid tumors because those originating in the brain or spinal cord rarely spread to other parts of the body. More than 35,000 of these primary tumors are diagnosed each year,¹ 16,500 of which are cancerous.² It has been

estimated that as many as 170,000 people develop metastatic tumors each year from cancer cells that have migrated to the central nervous system from a primary tumor elsewhere in the body. CNS tumors in children often form in different areas and come from different cell types than those in adults, and children's tumors may have a different prognosis and treatment. CNS tumors of all types cause approximately 13,000 deaths each year.

The outlook for a person with a brain or CNS tumor can depend almost as much on the tumor's location as its type. For example, a slow-growing ("benign") tumor can become life-threatening if it begins to crowd a crucial area of the brain and cannot be removed or treated, while a more aggressive tumor that is in a less

critical location or more easily treated may pose less threat.

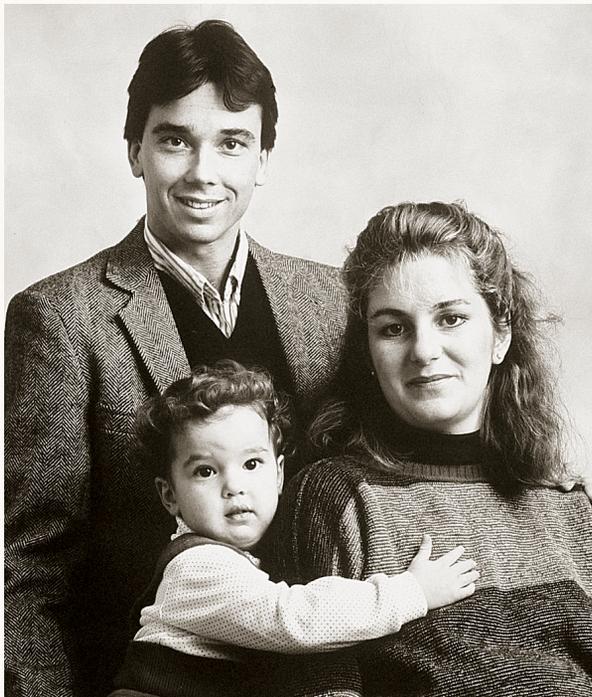
My brain tumor was discovered after I had a seizure, but I've learned people can have a variety of symptoms.

Symptoms vary markedly depending on the tumor's type and location. Headaches (particularly morning headaches),

seizures, and mental changes such as memory, speech, and communication problems are symptoms that may signal a CNS tumor, or may be related to other medical conditions. Similarly, some people with tumors that are causing excess pressure in the skull may experience nausea or vomiting, blurred or double vision, hearing disturbances, or problems with muscle control or coordination. These symptoms, too, may be related to other medical problems.

The doctor was able to remove most of my tumor, and we're treating the remaining part with radiation. I'm also going to try a new type of chemotherapy, but I know it may not get rid of my tumor forever.

Continuing advances in imaging technologies are improving our ability to diagnose CNS tumors and remove them more safely. Currently, magnetic resonance imaging (MRI) is the preferred method for diagnosing many types of CNS tumors, but computed tomography (CT) is often used because it is more widely available and less expensive. Positron emission tomography (PET) is one of several other scans now used to augment MRI or CT, but these other scans require the use of scarce equipment and are costly. Researchers are evaluating new, non-invasive modalities for tumor assessment, such as magnetic resonance spectroscopy (MRS), which is available with routine MRI equipment. Image-guided surgery has improved the surgeon's ability to remove tumor tissue without interfering with crucial brain functions. New techniques such as functional MRI



that shows brain areas involved in motor control, sensory function, language, and other functions, are improving surgical precision even further.

After surgery, many patients are treated with radiation. Several types of radiation therapy are available, including conventional external beam radiation, and both stereotactic radiotherapy and intensity modulated radiation therapy (IMRT), which are used to treat very small, multiple, and hard to reach tumors. The gamma knife is a radiotherapy that may be used to treat certain tumors that are inoperable with conventional surgery.

Chemotherapy for CNS tumors has been hampered by problems in getting anti-cancer drugs across the blood-brain barrier, a network of vessels and cells that filter blood going to the brain. Researchers are developing new drug delivery techniques and new agents that can cross the blood-brain barrier. For example, agents have been developed that temporarily open the blood-brain barrier while chemotherapy is administered through a vein or artery, and biodegradable wafers filled with chemotherapy drugs can be placed directly into the tumor. Chemotherapy drugs now include those designed to kill tumor cells, those that inhibit the development of blood vessels that feed the tumor, agents that cause tumor cells to behave more like normal cells, drugs that keep tumors from invading normal tissue, and agents that control cell growth and enzyme production or action. Scientists also

are working on gene therapies for CNS tumors.

With my type of tumor – a low-grade astrocytoma – my doctor says my outlook is pretty good. I’m hoping that in the next few years they’ll have even better treatments for my cancer.

Research is underway on all types of brain and CNS tumors. In addition to developing new imaging techniques and treatments, scientists are working intensively to better understand the molecular and genetic changes that occur in CNS tumors. These discoveries will accelerate the development of better preventive and therapeutic interventions, and will improve our ability to detect CNS tumors and monitor their response to treatment.

I can’t help wondering what caused my brain tumor, but mostly I’m just trying to make the most of my life with my wonderful wife and our little girl.

The causes of CNS tumors are not well understood. Six inherited genetic syndromes have been associated with CNS tumors, but inherited genetic alterations are not believed to account for a large proportion of these tumors. Gene alterations that may lead to a CNS tumor can also be caused by environmental factors, but the evidence on most factors studied to date is inconsistent. One exception is that high-dose radiation used to treat brain tumors has been related to second CNS tumors in sur-

vivors who have undergone this type of treatment. However, low-dose radiation from diagnostic x-rays and workplace exposures have not clearly been found to increase risk of CNS tumors, nor has exposure to low energy electromagnetic fields (EMFs) or the microwave frequencies associated with cellular telephones. It appears that regular exposure to some categories of chemical agents (e.g., N-nitroso compounds, some pesticides) may increase the risk of CNS tumors, but more research is needed in this area. Similarly, researchers are exploring whether exposure to certain viruses may affect CNS tumor risk. But the majority of people with CNS tumors do not have any of these possible risk factors.

Most people living with CNS tumors have symptoms that may change over the course of their disease. An important area for further research is to learn how to help people cope most effectively with the physical and psychological impact of these diseases, and the possible short- and long-term side effects of their treatment.

This year, NCI convened a Progress Review Group on adult and childhood brain tumors to assess the current state of knowledge and care for this group of diseases, and identify research priorities for the future.

Note: This vignette is a composite of experiences.

1 Central Brain Tumor Registry of the U.S.

2 NCI Surveillance, Epidemiology, and End Results (SEER) cancer registry program.

NCI's Challenge: Building Our Capacity for the Future

We are entering the 21st century with ever-expanding knowledge and an array of sophisticated tools for continuing the fight against cancer. The challenge before us is to build and continually enhance an infrastructure that will allow the scientific community to apply new discoveries and emerging technologies. We need mechanisms that will promote and reward innovative thinking, the cross-fertilization of ideas among disparate scientific disciplines, and enhanced collaborations among government, academia, and industry. We must develop and maintain a cadre of trained scientists from a variety of disciplines. And we must address special societal concerns that impact our Nation's ability to provide the best possible treatment to cancer patients and to ensure equal access to information, to care, and to research opportunity.

NCI must provide the vision, creative environments, and diverse resources needed to ensure a

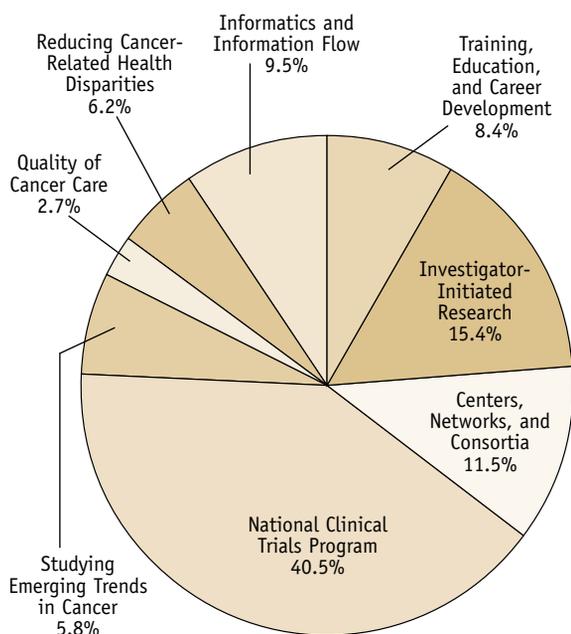
smooth flow between the increasing number of discoveries and advances in cancer research and the scientific community's ability to apply these findings. If the pace of discovery is like an eight-lane highway, our current ability to translate those discoveries into clinical application is still much like a country road. Where the two meet, a bottleneck still prevents a tremendous number of good ideas from moving forward. Our challenge is to continue to expand the country road and to move discoveries to their application in interventions across the cancer care continuum. To respond to this challenge, we identified six key areas for investment in our 2001 proposal and will continue these in 2002.

As we work to address this challenge, other barriers limit our success. Two issues of special concern are the quality of cancer care and disparities in access to information, patient care, and research opportunities and careers. We are adding two new challenge areas for 2002 to address these needs.

Budget Increase Request for 2002

(dollars in thousands)

Investigator-Initiated Research	\$124,561
Centers, Networks, and Consortia	93,500
National Clinical Trials Program	328,000
Studying Emerging Trends in Cancer	47,300
Quality of Cancer Care	21,500
Reducing Cancer-Related Health Disparities	50,600
Informatics and Information Flow	77,250
Training, Education, and Career Development	68,000
Total	\$810,711



Investigator-Initiated Research

THE CHALLENGE

Investigator-initiated research – research conceived and conducted by scientists in laboratories and clinics across the country and at NCI – is the wellspring of scientific discovery. Funded and sustained by a variety of NCI grant mechanisms, investigator-initiated research is continually yielding discoveries and insights into the mechanisms and causes of cancer and its prevention, detection, diagnosis, treatment, control, and survival.

Because of the steadfast national commitment to cancer research, scientists are beginning to understand how cancer develops and progresses at the molecular level and how to use this knowledge to effectively prevent, diagnose, and treat cancer. We now must not only maintain our current momentum but must push forward as quickly as possible with critical research and the application of findings to prevention and treatment interventions. The pace and absolute number of discoveries and the speed with which we can bring them to bear to benefit people, are directly linked to the resources available to support the exploration of new leads across the cancer research continuum. We must:

- Expand our research portfolio to include a greater number of proposals that may be somewhat speculative or that pursue novel paths.
- Continue to expand the translational research that converts basic science discoveries into practical, affordable, and effective ways of restoring cancer patients to health and preventing cancer throughout our population.
- Create mechanisms that link basic, clinical, and population-based research with state-of-the-art resources and technologies; promote collaborations among researchers inside and outside of cancer research; and draw into cancer-related research scientists from allied fields such as

chemistry, biology, physics, engineering, and mathematics to galvanize their complementary knowledge and most quickly answer the crucial questions in basic, clinical, population, and translational research.

The Nation waits eagerly for the day when cancer is no longer a threat to health and life, when most cancers are prevented, and when those that occur are cured or controlled rapidly and successfully. Meeting this challenge requires increased investment in this essential aspect of the research infrastructure, to span the gap between discovery and application and transform the processes by which we bring discoveries to the benefit of people.

G O A L

Accelerate discoveries and their application by expanding and facilitating researcher access to resources and new technologies.

PROGRESS TOWARD MEETING THE CHALLENGE

Over the past four years, NCI has increased substantially the number of investigator-initiated grant applications funded. In 1995, the overall success rate for grants funded from the Research Project Grant (RPG) pool was 23 percent. In 2000, we anticipate fund-

ing approximately 1,175 new and competing grant applications from the RPG pool, for an overall success rate of 30 percent. This increase has resulted in and will continue to yield substantial research rewards, but this improved funding level is still insufficient to support the wealth of innovative, high quality proposals received each year. As we achieve success in attracting new researchers to the cancer problem, the number of excellent applications is expected to grow.

To encourage the development of new technologies and innovative approaches to areas with special needs, NCI has implemented several new or expanded mechanisms. For example, the **Quick-Trials** program promises to speed the translation of ideas developed in the laboratory to early stage clinical trials by simplifying the grant application process and provid-

THE PLAN – INVESTIGATOR-INITIATED RESEARCH

Goal

Speed the rate of discovery and accelerate the application of those discoveries to the population by expanding and facilitating researchers' access to resources and new technologies.

Objectives and Milestones for Fiscal Year 2002

1. Increase investment in research to ensure a higher and sustainable success rate for competing grant applications.

- Fund 40 percent of competing applications, including those that: (1) have the highest scientific merit, (2) may have low probability of success but may yield potentially greater reward if they do succeed, (3) are unconventional but hold unique promise, (4) are in areas of extraordinary need in specific fields of investigation or model systems, or (5) encourage new investigators.

2. Encourage investigators to commit to careers in cancer research and to propose more innovative and higher reward projects.

- Continue to allocate the first 80 to 90 percent of available RPG funds to competing applications that fall within conventional merit rank order paylines.
- Ensure that applications that are particularly innovative and high reward have a reasonable funding rate by identifying such research and using exceptions funding and special competitions as warranted to maintain a comparable overall success rate.

3. Enhance the pace of high priority targeted research objectives by searching for outstanding applications that fall just beyond established paylines.

- Ensure that applications from new investigators have a success rate equal to grants from more established investigators.
- Allocate up to 10 percent of competing RPG funds for meritorious applications outside conventional paylines.
- Continue AER to fund single project applications in patient-oriented and basic research that are near the payline and for which reviewer criticisms can be addressed rapidly. Provide parallel expedited peer-review approaches for Program Project Grants.

4. Invest in areas that NCI consensus planning processes (e.g., progress review groups, extraordinary opportunity working groups, advisory committees) and staff have identified as presenting special opportunity or need.

- Set aside 10 to 15 percent of funds for Requests for Applications (RFAs), Program Announcements (PAs), and other applications that target identified gaps and/or emergent opportunities. Monitor investigator-initiated research applications to assess whether these projects alone are meeting programmatic objectives, including those focused on special needs identified in specific disease areas. Use regular, novel, and special award mechanisms to encourage investigation in priority areas.

- Provide sufficient staff, other resources, and enhanced electronic communications to improve information dissemination, enhance coordination within and among initiatives, and increase direct contact with applicants and grantees.

5. Optimize each award to accelerate the pace of discovery.

- Provide funding at full peer-reviewed recommended budget levels for up to five years of support. (See the NCI funding plan at cancer.gov/admin/fmb.)
- Ensure that investigators have access to NCI-sponsored resources, infrastructure, and technologies that facilitate discovery, both to expedite progress and to create breakthrough opportunities.
- Triple the amount of funding set aside for administrative supplements to current awardees whose research is going better than expected, or who are poised to test new ideas.
- Expand R03, R21, R33, P20 and other award mechanisms that provide seed funds and resources to pilot promising leads. (Go to deainfo.nci.nih.gov/flash/awards.htm#menu for information on NCI funding mechanisms.)

6. Facilitate rapid movement from discovery to application by encouraging transdisciplinary and collaborative approaches.

- Use established mechanisms and create novel and special awards to encourage collaborative and translational research.
- Expand administrative supplements to encourage new collaborations that bring together basic and clinical scientists and promote additional interdisciplinary collaborations and access to central resources such as databases, tissue banks, and animal models. Expand access to resources and technologies that promote interdisciplinary research and collaborations through centers, networks, and consortia. (See [pp. 30-31, Objective 2](#).)
- Expand cooperative resource programs (e.g., RAID, RAPID, CGAP, EDRN) that give investigators access to technologies and expertise needed to move their discoveries to application. (See [pp. 30-31, Objective 2](#); [pp. 78-79, Objectives 2 and 3](#); and [p. 84, Objective 2](#).)
- Encourage the development of information technology tools to foster and enhance interdisciplinary communication and collaboration.
- Double the funding for collaborative research awards such as Program Project Grants and cooperative agreements for networks in cancer genetics, imaging, early detection, and other areas.
- Expand use of exploratory grants to encourage patient- and population-based research.

Total
\$124.6 M

Investigator-Initiated Research

Unsolicited

Each year NCI receives over 8,000 applications for research funding covering virtually all areas of science and medicine relevant to cancer. The vast majority of these applications are unsolicited and come from researchers representing a wide range of disciplines driven by the synergism present at their medical schools, hospitals, universities, research centers, and corporations all across our nation and around the world. Proposals selected for funding by peer reviewers are those that (1) ask important questions, (2) present novel and technically advanced approaches, and (3) hold promise for advancing the state of knowledge in a particular area. The sheer number of applications and a stringent review process together generally result in a fairly balanced and comprehensive research portfolio focusing on all aspects of cancer-related science and technology.

Solicited

In addition, NCI's ongoing planning and evaluation processes serve to further identify imbalances, gaps, or opportunities. Set-aside funds are established to channel research support into areas not adequately covered through unsolicited proposals, and Requests for Applications and Program Announcements are issued to solicit proposals in these areas. Judicious use of funding solicitations can cut years off the time needed to develop a critical mass of research in an emerging field and may be used to jump start new initiatives, such as those developed to implement the "Extraordinary Opportunities" outlined in this document. And funding solicitations permit NCI to coordinate and facilitate collaboration across institutional boundaries. Set asides also serve to assure investigators that NCI will commit support for an area, even though a problem may not have fared well previously in peer review or may seem intractable because progress has been difficult to achieve.

ing a rapid turnaround from application to funding. Initially developed as a pilot program in prostate cancer, this successful initiative has been expanded to address all cancer sites and provide funding to test and develop novel cancer therapies.

The **Phased Innovation Awards** program, developed initially to support novel technology development for molecular analyses of cancer, will be broadened in scope in 2001 to fund projects to advance imaging technology. In addition, the Institute has expanded the Award to include a follow-on Phased Technology Application Award to ensure subsequent development towards an applied result. Seven grants were funded through this program in Fiscal Year 2000.

In 1999, NCI used the **Administrative Supplements for Advanced Technologies** awards to fund over 20 centers to develop DNA array technology facilities. These grants promise to make this exciting technology available to hundreds of investigators at least a year earlier than otherwise would have been possible.

Through a **special exceptions process**, NCI ensures that new investigators share the same success rate as more established applicants. In addition, the **Accelerated Executive Review (AER)** process ensures rapid reconsideration of applications ranked within a few percentile points of the payline, especially those involving patient-oriented research. In Fiscal Year 2000, over \$35 million has been spent on exceptions and more than 100 investigators benefited from these initiatives.

Budget Increase Request for 2002 Investigator-Initiated Research

1. Ensure a higher and sustainable success rate for competing grant applications.
2. Encourage careers in cancer research and more innovative and high reward projects.
3. Enhance the pace of high priority targeted research beyond established paylines.
4. Invest in areas identified as presenting special opportunity or need.
5. Optimize each research award to accelerate the pace of discovery.
6. Encourage transdisciplinary and collaborative approaches.

Total \$124.6 M

Centers, Networks, and Consortia

THE CHALLENGE

NCI's mission to translate scientific knowledge into more effective cancer interventions is challenged by the conventional ways research is conducted. Basic scientists, clinical scientists, population scientists, and behavioral scientists develop their skills in distinctly different ways and in varied environments with far too little emphasis on communicating and working with each other except in very select environments. However, the rapid pace of scientific and technological discovery is creating enormous opportunities that require the close interaction and collaboration of clinical and laboratory scientists from across the research community. The challenge for NCI is to create integrated research environments that foster the complex multidisciplinary interactions needed to address the "big picture" problems in cancer research.

These integrated research environments must functionally link basic, clinical, population, and behavioral scientists to each other and to newly developing, diverse fields of science and technology. These scientists must have easy access to many different patients and at-risk populations, tissue banks, new technologies, and state-of-the-art informatics. They must be able to work together with the same ease and flexibility in multi-institutional research settings as in the same institution.

To meet this challenge, NCI continues to create and nurture a new overarching structure for research composed of NCI-designated Cancer Centers, Centers of Research Excellence, networks, and consortia. These infrastructures are enhancing the traditional research enterprise in ways that promote and facilitate complex scientific interactions, provide the critical resources essential for the research, and encourage the easy exchange of information and ideas through new communications linkages.

NCI-Designated Cancer Centers

NCI-designated Cancer Centers organize and integrate multidisciplinary research across departments and schools within a single institution. Cancer centers provide scientists access to the most advanced technologies and new research opportunities and bring the benefits of their research directly to the public. They link state-of-the-art research and clinical care activities within the institution and form key partnerships with industrial, community, and state health organizations outside of the institution. For example, the disease-specific Specialized Programs of Research Excellence (SPORes), designed to move discoveries from the laboratory into patient and population research settings, had their origins in cancer centers. The new Special Populations Networks for Cancer Awareness Research and Training are designed to link local, community, and regional problems of cancer in underserved populations to the broad-based research capabilities of NCI-designated Cancer Centers. Centers are critical in a new NCI initiative to incorporate Minority Serving Institutions (MSIs) into

NCI's cancer research, education, training, and outreach activities. The Cancer Genetics Network (CGN) sites are headquartered in centers. Nearly all of the participants in the Mouse Models of Human Cancer Consortium (MMHCC) are in NCI-designated Cancer Centers. Centers have worked closely with industry in developing new cancer therapeutic agents and are rapidly becoming significant partners with industry for new technology development.

NCI will create Regional Enhancement Cancer Centers to facilitate partnerships between smaller institutions and the large, existing NCI-designated Comprehensive Cancer Centers. These partnerships will provide patients and populations with much improved access to the newest clinical,

G O A L

Create and sustain research infrastructures for collaboration, technology support and development, and access to resources.

THE PLAN – CENTERS, NETWORKS, AND CONSORTIA

While the NCI's goal for collaborative research applies to all NCI-designated Cancer Centers, networks, and consortia, this plan focuses primarily on the objectives and resources for the centers and SPOREs. Many networks and consortia activities are budgeted and discussed in the Extraordinary Opportunities and NCI Challenge sections throughout this document.

Goal

Create and sustain research infrastructures for collaboration, technology support and development, and access to resources that enable multiple scientific disciplines to address large problems in cancer that could not be solved by individual investigators.

Objectives and Milestones for Fiscal Year 2002

- 1. Increase the number and broaden the geographic distribution of NCI-designated Cancer Centers. \$15.0 M**
 - Designate 2 new cancer centers. \$2.50 M
 - Award 2 new Cancer Center Planning Grants. \$0.50 M
 - Establish 3 Regional Enhancement Cancer Centers that will collaborate with NCI-designated Comprehensive Cancer Centers to expand the base of patients and populations available for early detection, prevention, and therapeutic research studies. \$2.00 M
 - Award 5 Cancer Center Supplements to encourage inter-center research collaborations when patient, community, and regional responsibilities are in competition or when combining resources can address important questions more effectively. \$3.00 M
 - Establish formal affiliations between cancer centers and MSIs in the form of 2 comprehensive partnerships, one planning grant for a comprehensive partnership, and 10 planning grants to increase the number of minorities engaged in cancer research, enhance research capabilities of MSIs, and improve the effectiveness of cancer centers in serving minority communities. (See [p. 59](#), Objective 4 for the training component of these partnerships.) \$7.00 M

- 2. Expand the capacity of cancer centers to engage in newly developing areas of research and technology and to act as platforms for translating discoveries into interventions. \$36.0 M**
 - Establish 10 Advanced Technology Programs in cancer centers to enable work with industry to develop, access, and export the newest technologies for solving important problems in cancer research. \$7.50 M

prevention, and control trials in early detection, prevention, and therapeutic research. NCI anticipates that the centers also will play a key role in integrating and coordinating NCI-supported centers of excellence, networks, and consortia into one overarching, unified research framework. Go to cancer.gov/cancercenters for more information.

Centers of Research Excellence

Centers of Research Excellence bring together interdisciplinary and translational research teams focused on a specific disease, modality, biologic process, or scientific area. They are awarded sizeable amounts of flexible funding to enable them to rapidly address emerging scientific opportunities.

- Increase funding to all cancer centers to encourage scientists in centers to develop new technologies and methodologies for entirely new approaches to answering important cancer research questions. \$6.00 M
- Establish 10 Informatics Planning Activities in cancer centers to build, in partnership with NCI, critical informatics capabilities in data acquisition, analysis, integration, and coordination. \$7.50 M
- Provide additional funding to build the clinical research and population research infrastructure of cancer centers. Fund databases that conform to NCI's clinical informatics infrastructure, support population studies, and provide more core staff to conduct innovative translational therapeutic and prevention trials. \$15.00 M

3. Expand and enhance the research of Specialized Programs of Research Excellence (SPOREs). \$31.0 M

- Expand the SPORE program scope to include one in breast cancer and one in prostate cancer. Add the following SPOREs: 2 in head and neck cancer, one in brain cancer, and one in lymphoma. Continue implementing the transition plan to include all cancer sites by Fiscal Year 2005. \$25.00 M
- Provide supplements to SPOREs for planning and developing complex inter-SPORE research projects and for collaborative projects with other NCI centers of research excellence, networks, and consortia. \$5.00 M
- Support development of an Internet platform and research database to enable SPOREs to exchange research results and to foster communications for sharing resources and developing collaborative inter-SPORE research projects. \$1.00 M

4. Develop a system for linking and managing the entire research framework of centers, centers of research excellence, consortia, and networks. \$10.0 M

- Create a flexible management system for planning, initiating, and completing complex collaborative research projects that provides for specialized short-term resources and research support. \$5.00 M
- Develop a communications network to identify areas of common interest, share research information and resources, develop a continuing research dialogue, and identify areas of potential collaboration. \$5.00 M

Management and Support

\$1.5 M

Total

\$93.5 M

The first of these centers, the SPOREs, were created in 1992 and focused on specific cancers. They serve as highly effective hubs for translational research, moving discoveries back and forth among laboratory, clinic, and population research settings. To date, SPOREs have been established in breast, prostate, lung, gastrointestinal, and ovarian cancer.

The SPOREs blueprint has been used to establish similar programs in other extraordinary opportunity research areas including Transdisciplinary Tobacco Use Research Centers, *In Vivo* Cellular and Molecular Imaging Centers, and Interdisciplinary Research Teams for Molecular Target Assessment. All of these support interactive,

multidisciplinary research and provide resources, flexible exploratory funds, training, and career development. NCI also will collaborate with the NIH Center for Complementary and Alternative Medicine to establish centers of excellence.

Networks and Consortia

Networks and consortia link the expertise and innovation of scientists from different disciplines and diverse research backgrounds to address important questions and issues about cancer. The CGN addresses the issue of inherited predisposition to cancer and is linking its goals and objectives to those of SPOREs and NCI-designated Cancer Centers. The newly established MMHCC will work closely with SPOREs to develop mouse models that reflect various precancerous and cancerous stages of human cancer. The Diagnostic Imaging Network, a multi-institutional team of scientists, is evaluating and developing a new generation of imaging concepts and tools with device manufacturers and other technology developers. The Early Detection Research Network, which facilitates the discovery, development, and initial steps in clinical validation of molecular markers and assays that detect early signs of cancer, is already interacting with SPOREs and other interdisciplinary teams of scientists. The SPNs will involve underrepresented racial, ethnic, and minority communities in establishing research priorities and conducting research that will benefit these populations. The Pediatric Brain Tumor Consortium, a network of 10 medical centers, is evaluating promising treatments for children with brain malignancies.

Networks and consortia interact with NCI-designated Cancer Centers and Centers of Research Excellence in a seamless way to advance our understanding of cancer and to improve cancer prevention, early detection, diagnosis, and treatment.

PROGRESS TOWARD MEETING THE CHALLENGE

NCI is completing the foundation for overarching research frameworks that will bring diverse scientific disciplines together across institutional boundaries. **NCI-designated Cancer Centers** continue to evolve as key strategic partners of NCI. In

2000, NCI added a center in Iowa and will fund a new planning grant for developing a center in New Mexico. In addition, the number of cancer centers with the “Comprehensive” designation increased in 2000 to 37. Finally, NCI has been working with institutions in Georgia, New York, Louisiana, Rhode Island, Florida, West Virginia, Kentucky, Arkansas, South Carolina, and Michigan to develop cancer centers or become **Regional Enhancement Cancer Centers**.

In 2000, the **SPORE program** added a new cancer site and funded four ovarian cancer SPOREs. These research teams already are establishing research links and preparing to conduct inter-institutional research that cannot be accomplished through any other venue. In addition, the SPORE program has become open to all types of cancer through a transition plan that will gradually add new cancers over the next five years. By the end of Fiscal Year 2001, NCI expects to support SPOREs in breast, prostate, lung, ovarian, genitourinary tract, gastrointestinal tract (pancreatic and colorectal), and skin cancers.

NCI recently launched the **Minority Institution/Cancer Center Partnerships (MICCPs)** to engage minority institutions in NCI’s research activities, including training, education, and community outreach. The program will engage five major institutions with medical schools (Drew, Meharry, Howard, Morehouse, and the University of Puerto Rico) and also will provide opportunities for over 300 other smaller institutions throughout the Nation to partner with NCI-designated Cancer Centers.

Budget Increase Request for 2002 Centers, Networks, and Consortia

1. Increase the number and broaden the geographic distribution of NCI-designated Cancer Centers.	\$15.0 M
2. Expand the capacity of cancer centers to engage in newly developing areas.	36.0 M
3. Expand and enhance SPOREs.	31.0 M
4. Develop system for linking and managing entire research framework.	10.0 M
Management and Support	1.5 M
Total	\$93.5 M

National Clinical Trials Program

THE CHALLENGE

During the 1990s, the number of new cancer preventive, diagnostic, and therapeutic agents tested in clinical trials increased dramatically. New cancer interventions in development by industry increased threefold to over 350. In 2000, NCI added to existing trials on 80 promising interventions for treatment and 35 for prevention, 30 more agents identified through its own drug discovery programs or in collaboration with academic institutions or industry.

But our present clinical trials system cannot keep pace with the growing number of agents that merit testing. As potential prevention and treatment strategies emerge from early clinical testing, NCI is faced with a backlog of agents that need to enter large Phase III trials, the final crucial step in translating new discoveries into effective new treatments and prevention strategies for patients. NCI and its grantees are able to initiate only about 30 Phase III treatment trials each year. Compounding this problem is the fact that fewer than three percent of patients with cancer participate in the clinical trials that might define effective new treatment approaches. For a variety of reasons including limited access, lack of insurance coverage, patient-physician communication issues, and therapy choice, only about 20,000 patients enter Phase III trials each year. This means that it can take over four years just to recruit enough patients for the average Phase III treatment trial. Nearly 90 Phase II and III prevention trials also have been initiated, but progress in this area is limited by lack of methods such as the use of biomarkers to determine the effect of a preventive over a short period of time, lack of technologies to improve precision in characterizing precancerous lesions, and the growing

number and complexity of trials needed to determine the roles of a new generation of agents.

To more efficiently convert recent scientific discoveries into effective interventions, eliminate the backlog of agents for testing, and increase access for patients and individuals at risk, we must invest in, restructure, and increase the capacity of our national clinical trials program. While the time from initiation of clinical trials to Food and Drug Administration (FDA) approval has improved, the clinical development required to establish the best uses of new agents still occurs over a much longer period.

Changes to NCI's clinical trials system will increase the number of trials and the number of individuals who enroll in trials by easing the way for physicians to communicate with patients and enroll them in trials. Results of laboratory studies to determine why particular drugs are effective in some individuals and not in others will help tailor treatments for cancer patients and interventions for people at risk for cancer. These enhancements will speed the development of new agents and alleviate the backlog of treatments awaiting evaluation.

G O A L

Ensure that clinical trials address the most important questions in prevention and treatment and are broadly accessible.

Budget Increase Request for 2002 National Clinical Trials Program

1. Address compelling clinical questions.	\$ 16.5 M
2. Increase development and clinical testing of promising new agents.	279.5 M
3. Increase participation in clinical trials by patients, individuals at risk for cancer, and their physicians.	22.5 M
4. Reduce outcome disparities in special populations by increasing trials access.	4.0 M

Management and Support	5.5 M
Total	\$328.0 M

THE PLAN – NATIONAL CLINICAL TRIALS PROGRAM

Goal

Ensure that the clinical trials program is poised to address the most important medical and scientific questions in cancer prevention and treatment quickly and effectively through state-of-the-art clinical trials that are broadly accessible to cancer patients, populations at risk for cancer, and the physicians who care for them.

Objectives and Milestones for Fiscal Year 2002

\$16.5 M

1. Identify and address compelling clinical questions confronting physicians and their patients struggling with cancer.

- Conduct State of the Science meetings in gastrointestinal, lung, genitourinary, and prostate cancers and leukemia to identify important research questions and define a scientific research agenda to address them. \$1.00 M
- Expand Concept Evaluation Panels beyond initial lung and genitourinary cancer pilots to include peer review of all concepts for Phase III trials sponsored by NCI. \$0.50 M
- Provide scientific leadership funds to support researchers who chair studies and statisticians responsible for writing, monitoring, and analyzing NCI-sponsored, high-priority Phase III trials. \$3.00 M
- Provide translational research funds for clinical correlative studies to uncover the mechanisms of action, response, and resistance underlying new treatments and preventive strategies and to translate basic biology from the laboratory to clinical practice. \$8.00 M
- Support a national tissue resource system that includes normal, precancerous, and cancer tissues to facilitate rapid evaluation of new assays and relevant clinical correlations as new targets are identified. (See [p. 78, Objective 2.](#))
- Fund tissue and specimen banks to store material from cancer patients undergoing treatment and those at risk of developing cancer to allow later studies of drug effectiveness, molecular abnormalities, and clues to tumor initiation and progression. \$4.00 M
- Develop and make widely available through Centers of Research Excellence molecular assays required to characterize/classify tumors. (See [pp. 30-31, Objective 2.](#))
- Better integrate treatment and prevention research into the clinical trials infrastructure.
- Incorporate behavioral, epidemiologic, outcomes and other relevant research, to effectively address cancer in specific tumor types and patient populations.
- Incorporate the evaluation of relevant biomarkers into clinical trials.

2. Increase the pace of development and clinical testing for promising new therapeutic and preventive agents.

\$279.5 M

- Over 2-3 years, triple the number of promising agents entering NCI-sponsored clinical trials, triple annual patient accrual to early clinical trials of promising agents, quadruple accrual to pivotal or proof-of-principle early clinical trials, and double accrual to Phase III clinical trials.
- Expand resources for the RAID and RAPID programs. (See [p. 84, Objective 2.](#))
 - Increase funding for early therapeutics development contracts to fund multi-institutional consortia that are able to accrue many patients rapidly and perform sophisticated correlative laboratory studies. \$13.00 M

<ul style="list-style-type: none"> ■ Fund Interdisciplinary Research Teams in Interventions Directed at Molecular Targets to develop the necessary assays, tools, and approaches to assess the effects of promising new agents on their molecular targets. \$6.50 M ■ Fund Cooperative Groups and practice sites to support data management and allow physician participation in clinical trials at double to triple the current rate through the CTSU. \$245.00 M ■ Support a rapid grant review process for mechanism-based clinical trials. ■ Support the infrastructure needs of the intramural clinical trials program at the NIH Clinical Center by increasing the numbers of data managers, research nurses, biostatisticians, and clinicians required to support a critical mass of clinical investigators; continue to develop the net-Trials database system to link all NCI intramural clinical investigations and as a prototype that other institutions can use; and continue the Tissue Array Research Program (TARP) to identify key molecular alterations in cancers. \$15.00 M 	
<p>3. Substantially increase participation in clinical trials by patients, individuals at risk of developing cancer, and the physicians who care for them.</p> <ul style="list-style-type: none"> ■ Use the EPP to fund new participating physicians, including new minority physicians, to hire the necessary research nurses and data managers for effective trials participation. \$2.50 M ■ Expand the CTSU to consolidate all administrative tasks associated with clinical trials. \$20.00 M ■ Provide extensive information about prevention and treatment options and clinical trials to enable patients and physicians to make informed medical choices. (See pp. 54-55, Objective 2.) ■ Develop uniform data reporting mechanisms and informatics support to facilitate clinical trials participation. (See p. 55, Objective 3.) 	\$22.5 M
<p>4. Reduce outcome disparities in special populations by increasing access to state-of-the-art clinical trials in cancer prevention and treatment.</p> <ul style="list-style-type: none"> ■ Create a Clinical Trials Outreach Program to increase participation by underrepresented populations; establish clinical trials units at historically black medical institutions; strengthen clinical trials units at minority-based community oncology sites. \$3.00 M ■ Increase clinical trials participation by minority physicians and health professionals by implementing an NCI fellowship training program in clinical trials for minority physicians and forums for minority scientists' input into developing clinical trials that address issues of special importance for minority and special populations. \$1.00 M 	\$4.0 M
<p>Management and Support</p>	\$5.5 M
Total	\$328.0 M

PROGRESS TOWARD MEETING THE CHALLENGE

We are finding better ways to generate new ideas. State of the Science Meetings identify disease-specific research gaps and opportunities, advance findings into clinical evaluation, and stimulate integrated translational research. Pilot Concept Evaluation Panels evaluate Phase III clinical trial proposals. The Quick-Trials program simplifies procedures and provides rapid turnaround for the funding of clinical trials on new agents and therapeutic approaches. The Clinical Oncology Special Emphasis Panel provides the clinical oncology community with its own NIH study section for reviewing clinical trials and translational research. Clinical correlative science studies will deepen our understanding of the relationship between tumor characteristics and patient outcomes.

We are broadening access to trials. Funding for Cooperative Groups, through which most patients enter clinical trials, has increased over 50 percent since 1999. The Expanded Participation Project (EPP) extends access to NCI-sponsored Cooperative Group studies to oncologists who are not Group members. Special Populations Networks for Cancer Awareness Research and Training have raised the proportion of minorities participating in treatment trials to nearly 20 percent. A Physician Communication Module developed with the Howard University Cancer Center will provide tools and technology for physicians to enroll and follow patients on clinical treatment protocols. NCI's payer and provider partnerships with the Department of Defense TRICARE/CHAMPUS health care system and the Department of Veterans Affairs provide coverage for trials participation by military personnel and veterans. Agreements with health plans such as Aetna-U.S. Health Care and United Health Care Corporation cover costs for patient care in trials. Medicare beneficiaries are now guaranteed coverage for participation in clinical trials as a result of a presidential directive in June 2000.

We are communicating and educating people about trials. The Cancer Clinical Trials Education Program provides training to nurses and social workers to educate patients and their families about clinical trials. We are partnering with professional societies and health plan organizations to develop Web-based and self-paced modules about clinical tri-

als participation for physicians and nurses. In collaboration with other NIH institutes and national ethics groups, NCI is developing a Web-based Human Subjects Protection Education program for investigators. Two Web sites provide extensive information on clinical trials to physicians and patients. CancerNet (cancer.net.nci.nih.gov) hosts NCI's searchable clinical trials database containing information on over 1,800 active clinical trials, and cancerTrials (cancertrials.nci.nih.gov) is NCI's online gateway to clinical trials resources. The latter integrates information about clinical trials participation (including human subjects' protection), treatment advances, and related resources for patients and physicians. The Cancer Trials . . . Because Lives Depend On It project is testing a new approach to participant accrual where partner organizations recruit "campaign ambassadors" to training programs and encourage their communities to participate in trials. New Minority Clinical Oncology Awards provide underrepresented minority health professionals with the opportunity to gain expertise in research.

We are streamlining procedures and automating data systems. The Cancer Trials Support Unit (CTSU) streamlines and centralizes administrative, financial, and data collection tasks. The submission and development of ideas for protocols are made easier through electronic forms, templates, and databases. A Central Institutional Review Board (IRB) is available to review protocols for multi-center trials, reducing the administrative burden on individual institutions. An informed consent template improves patient understanding of cancer trials participation. The Clinical Trials Monitoring Branch Audit Information System permits online submission of data collected during quality assurance audits. The Clinical Data Update System will standardize and streamline data reporting and reduce administration. Common Data Elements and Common Toxicity Criteria promote a common vocabulary among cancer research organizations. The Adverse Event Expedited Reporting System is a Web-based system for reporting to NCI serious or unexpected events.

We continue new initiatives through our Intramural Clinical Program including: a new program in neurooncology/brain tumor research in collaboration with the National Institute on Neurological Disorders and Stroke, expansion of the cDNA Microarray Facility to support clinical research for finding new biomarkers, the Tumor

Harnessing the Immune System to Prevent and Treat Cancer

Over the past century we have gained considerable knowledge about how the immune system fights off foreign invaders and how cancer eludes this defense system. The application of this knowledge to creating immunotherapies, such as immunotoxins and vaccines that harness the immune system, is yielding promising results for both treating and preventing cancer.

Recent research shows that an immunotoxin (LMB-2), a type of treatment created by linking a monoclonal antibody to a deadly toxin, may be effective against hairy cell leukemia (HCL), a rare cancer of immune system B cells. When given to a patient, the antibody portion of LMB-2 homes in on a cancer cell, attaches to it, and then delivers its poison directly to the cell, thus killing it. In a phase I clinical trial of LMB-2, NCI researchers saw anti-tumor activity against a variety of malignancies including chronic lymphocytic leukemia, Hodgkin's disease, cutaneous T-cell lymphoma, and most strikingly, HCL. Four out of four HCL patients who received LMB-2 responded to the treatment. One patient had a complete remission that has lasted almost two years and the other three patients had a reduction of 98 percent or more in malignant cells circulating in the blood. Phase II trials of LMB-2 will begin soon.

Vaccines are another type of immunotherapy. Prevention vaccines, like the polio vaccine or childhood immunizations, evoke an immune response before infection strikes, creating antibodies that will later ward off a challenge. Prevention vaccines for cancer are similarly designed to target cancer-causing agents, such as the sexually transmitted human papillomavirus (HPV) which is linked to over 90 percent of cervical cancer cases worldwide. HPV is now believed to cause some types of oral cancers, too, such as tumors found in the tonsils. Researchers are hoping that inoculation with inactivated HPV particles will enable the immune system to recognize and establish a defense against the virus. Worldwide, at least six vaccines with potential to pre-

vent HPV infection are being developed and tested. NCI has launched early clinical trials of a vaccine that creates a protective effect by employing virus-like particles from HPV-16, the form of the virus involved in over 50 percent of cervical cancer cases. Preliminary results show that a low-dose injection of the vaccine induces high levels of protective antibodies against HPV. Future clinical trials may include oral cancer patients. In addition, NCI-funded scientists are working on creating a vaccine that contains virus-like particles from the four major strains of HPV that together contribute to more than 80 percent of all cervical cancers.

Unlike the HPV vaccine, most cancer vaccines are designed to treat existing cancers by inducing an immune response that leads to a direct attack on tumor cells. For example, researchers have developed and are testing a B-cell lymphoma vaccine that primes a patient's immune system to seek out and destroy tumor cells. To create this vaccine, scientists removed tumor cells from a patient's lymph nodes and selected and isolated a protein present only on the cancer cells. The isolated protein was then joined to a carrier protein that could transport it into the body and aid in creating an immune response. Finally, an immune system boosting drug was added to the vaccine combination for maximum effect. Of the 20 patients injected with custom-made vaccines as part of a small Phase II trial, 18 remained in complete remission an average of four years. A large-scale trial of the vaccine involving 390 patients has now been launched.

Immunotherapy research has proven that the immune system can be primed to recognize and destroy tumor cells with minimal toxicity compared with chemotherapy and other treatments. Thus, immunotoxins and vaccines are a positive addition to our arsenal of anti-cancer therapies, but additional clinical trials are needed to help us maximize their potential.

Vaccine Program through which NCI is initiating clinical trials to test the efficacy of anti-lymphoma and anti-melanoma vaccines, and the Radiation Oncology Sciences Program for linking intramural and extramural initiatives in improving radiation

treatment. Intramural researchers also are exploring new imaging approaches to cancer.

For more information on the cancer trials revitalization efforts described here, go to cancertrials.nci.nih.gov and select "New Trials System."

Studying Emerging Trends in Cancer

THE CHALLENGE

Identifying and tracking rates and trends in cancer and monitoring the factors that influence these changes are crucial underpinnings of efforts to prevent and control cancer. Reduction in the cancer burden is a critical measure of the progress we are making against cancer. Since 1990, new cancer cases and death rates have fallen for all cancers combined and for most of the top ten cancer sites, reversing a decades-long trend of rising cancer incidence and death rates in the United States. These decreases support the wisdom of the Nation's investment in cancer research.

Appropriate decision making in science and in public health depends on accurate, reliable information about the incidence and impact of disease. NCI's Surveillance, Epidemiology, and End Results (SEER) cancer registry program provides data to identify and study variations in cancer rates, assess trends, track the impact of cancer on the general population, and provide information that researchers need to ask critical questions about why certain populations are affected by cancer more severely than others. SEER data have enabled us to identify environmental carcinogens, monitor cancer-related effects of tobacco, identify geographic areas with higher than average cancer rates, study patterns and outcomes of cancer care, and identify risk groups for research and public health intervention programs.

Recent changes in health care financing and delivery, the revolution in informatics and computer programming technology, and the social and cultural diversity of our country present new challenges and opportunities in surveillance research. Currently, our understanding about how risk factors, screening, and treatment may affect trends in the cancer burden is beginning to unfold, and advancing

knowledge in these areas will require new data sources and statistical methods. In addition to the incidence and mortality data now collected, research is needed to improve methods for measuring quality of life, quality of care, health status, morbidity, family history, cancer risk behaviors, screening, and treatment. Better methods and models also are needed for relating these measures, quantifying their impact on current and future cancer rates, and predicting outcomes.

New investments are required to support the adoption of tools that will improve the precision and expand the reach of our cancer surveillance efforts. These include geographic information systems that allow data linkage and statistical analysis of individuals and potential environmental exposures by location, new approaches to modeling trends, and more refined cancer maps and spatial statistical techniques for assembling, analyzing, and disseminating surveillance data.

NCI's surveillance efforts should be expanded to cover the spectrum of racial, ethnic, socioeconomic, and cultural diversity. New investments in research on specific population groups will allow us to connect information on prevention, risk factors, screening, treatments, and patterns of care with outcomes such as incidence, quality of life, and mortality.

Greater efforts are needed to disseminate the results of NCI's surveillance research to scientists, the general public, and policy makers. As the field of surveillance research expands and takes on these new challenges, it is clear that scientists with skills encompassing the disciplines of epidemiology, statistics, disease registration, geographic information systems, and informatics are in short supply. NCI must create the training opportunities necessary to prepare the next generation of surveillance researchers. Enhancing our investment in surveil-

G O A L

Expand cancer surveillance to improve monitoring of progress in cancer control and explain potential causes of cancer across all populations.

lance research will ensure that NCI continues to play an active and visible national leadership role in developing a comprehensive national surveillance program.

PROGRESS TOWARD MEETING THE CHALLENGE

The **Cancer Surveillance Series**, developed by NCI scientists and the editorial staff of the *Journal of the National Cancer Institute*, makes information about factors contributing to cancer more accessible to researchers and the public. These published research articles address emerging patterns of cancer in various population groups and explore the elements affecting these patterns at the national and regional level. Begun in June 1999, the series provides a forum for disseminating the latest analysis and evaluation of U.S. cancer statistics, with special emphasis on data from population-based SEER cancer registries. Similarly, NCI recently published the **Atlas of Cancer Mortality in the United States, 1950-1994**, showing geographic patterns of cancer death rates in over 3,000 counties across the country. Available on the Web (cancer.gov/atlas), the 254 color-coded maps make it easy for researchers, public health professionals, and health departments to more precisely identify places with high or low cancer rates, and uncover cancer patterns.

To better understand the burden of cancer in various populations, NCI is **expanding its cancer surveillance program** to cover a broader spectrum of the racial, ethnic, socioeconomic, and cultural diversity. In 1999, coverage of Alaska Natives was added to the SEER program, and steps were taken to improve the quality of data on American Indians. NCI now is expanding SEER to enhance coverage of rural whites and blacks, non-Mexican Hispanics, American Indians, and states with high cancer death rates. Collaborative studies such as the **National Longitudinal Mortality Study** involving the NIH, the Census Bureau, and the National Center for Health Statistics (NCHS) were launched in 1999 to improve cancer mortality data for racial, ethnic, immigrant, and socially disadvantaged populations. These studies will make it possible to connect important socioeconomic and demographic information with prevention, risk fac-

tors, screening, treatment, and patterns of care in special populations.

Computer software known as **SEER Stat**, developed by NCI, makes it easier for people to use SEER data. The software is provided free of charge on SEER public use files, more than 1,500 of which are being distributed each year. A database management system for SEER cancer registries is being developed to support registry operations and promote more uniform standards and consistency among U.S. population-based cancer registries.

A **Cancer Control Topical Module** is being fielded in collaboration with NCHS as part of the National Health Interview Survey (NHIS). This module provides critical national data for tracking progress in major cancer control health practices. Similarly, NCI is partnering with the California State Department of Public Health to initiate a new state-level survey similar to the NHIS, the **California Health Interview Survey** (www-dccps.ims.nci.nih.gov/ARP/RiskFactor/chis.html). A decade of data related to monitoring progress in tobacco control in all states and the District of Columbia has been made available as a public use file with the **Tobacco Use Supplement to the Current Populations Survey** (www-dccps.ims.nci.nih.gov/ARP/RiskFactor/tobacco.html). Seven centers and a statistical coordinating center were funded this year to continue support of the **Breast Cancer Surveillance Consortium** (BCSC – www-dccps.ims.nci.nih.gov/ARP/breastcancer.htm). The BCSC, established to enhance our understanding

Budget Increase Request for 2002 Studying Emerging Trends in Cancer

1. Improve cancer registry data.	\$11.8 M
2. Expand systems and methods to enhance the quality of cancer control data.	25.0 M
3. Expand systems and methods to enhance capacity for exploring causes of cancer, generating new hypotheses, and identifying new opportunities.	5.0 M
4. Improve and expand training in surveillance research and improve dissemination of information.	3.5 M
Management and Support	2.0 M
Total	\$47.3 M

THE PLAN – STUDYING EMERGING TRENDS IN CANCER

Goal

Expand surveillance data systems, methods, communications, and training to improve capacity for monitoring progress in cancer control and for explaining potential causes of cancer nationally and among diverse populations.

Objectives and Milestones for Fiscal Year 2002

1. **Improve cancer registry data by expanding SEER coverage, improving the quality of all population-based cancer registries, and enhancing SEER as a research resource.** **\$11.8 M**
 - Support 2 to 5 new SEER registries to improve coverage of key populations: non-Mexican Hispanics, residents of Appalachia and other rural areas (especially those of lower socioeconomic classes), rural African Americans, American Indians, and populations with high cancer mortality rates. \$6.00 M
 - Provide funding for technical assistance, quality control, and special studies to improve operational efficiency and data comparability among population-based cancer registries. Support field and analytic audits; training and fellowship programs; methodology development; linkage with other health-related information sources; and development of more efficient technology-based information systems. \$2.00 M
 - Expand support for applied innovations in SEER population-based cancer registry data systems, including portable modules to facilitate cost-effectiveness, improve methodology, and advance research in newly diagnosed patients. \$0.80 M
 - Develop a biospecimen resource for archived tissue for population-based surveillance and epidemiologic research. Support on-staff pathologists, tissue accession managers, and administrative personnel to coordinate response to approved requests for specimens. \$3.00 M

2. **Expand systems and methods to enhance the quality of cancer control data on risk, health and behaviors, and screening practices linked to high quality data on cancer outcomes.** **\$25.0 M**
 - Build a surveillance system to monitor progress in tobacco control. (See [p. 88](#), Objective 1.)
 - Enhance national and regional data systems to measure health disparities in cancer-related health behaviors and screening practices. Expand support for cancer control supplements to national and regional surveys and enhance data on socioeconomic and other demographic factors associated with disparate cancer outcomes. \$8.00 M
 - Fund surveillance screening consortia to assess cancer screening performance at the community level. Continue efforts to examine mammography screening quality through the BCSC, begin a comparable research consortium in colorectal cancer screening, and examine the need to establish comparable consortia to evaluate screening quality for cervical and prostate cancers. \$10.00 M
 - Supplement existing surveillance screening consortia and population research networks, such as the Cancer Research Network, to examine emerging issues in cancer control including obtaining data on barriers to entry into cancer clinical trials, expanding cancer screening surveillance in specific ethnic or at-risk populations, and examining the effect of tobacco and food-related policy and legislation. \$2.00 M

<ul style="list-style-type: none"> ■ Fund data collection and research on prognostic risk factors, health behaviors, quality of life, and cancer care processes. (See p. 46, Objective 2.) ■ Conduct SEER special studies to obtain similar cancer control and quality of care data within SEER registries. Explore the feasibility of obtaining specific cancer care data currently not collected as part of routine cancer registration. \$1.00 M ■ Develop new data linkages and expand support for analysis of linked data sets, such as the SEER-Medicare database, managed care and other sources of claims data, or other regional or national health surveillance data. \$2.00 M ■ Support statistical and methodological studies to improve accuracy and reliability of data on socioeconomic determinants of cancer rates and risk, health behaviors, and screening. (See p. 50, Objective 3.) ■ Develop statistical and graphical methods, software applications, and other technologies relevant to geospatial and mapping research. \$2.00 M 	\$5.0 M
<p>3. Expand systems and methods to enhance capacity for exploring causes of cancer, generating new hypotheses on risk, and identifying new opportunities for cancer control interventions.</p> <ul style="list-style-type: none"> ■ Fund epidemiologic research studies utilizing the <i>NCI Atlas of Cancer Mortality in the United States, 1950-1994</i> and other population-based data systems on cancer incidence, vital statistics, and vital records to identify potential new leads in cancer causation. \$2.50 M ■ Support research initiatives using geospatial, mapping, and other analytic methods applied to existing population-based systems of environmental, sociocultural, and other relevant risk factors to develop hypotheses for more in-depth studies of cancer causation. \$2.50 M ■ Support studies that use biospecimen resources from population-based cancer registries. (See p. 66, Objective 1.) 	\$5.0 M
<p>4. Improve and expand training in surveillance research and improve dissemination of information to researchers, public health professionals, the public, policy makers, advocates, and legislators.</p> <ul style="list-style-type: none"> ■ Fund existing surveillance and applied research networks and consortia to conduct intensive training programs, provide sabbatical opportunities for research professionals, and initiate and develop academic curricula on surveillance research. \$2.00 M ■ Improve surveillance data dissemination using emerging information technologies and the Internet for information exchange. Expand innovative dissemination, particularly visual representation of data, to improve its comprehension by non-technical audiences. \$1.00 M ■ Continue to produce the annual <i>NCI National Cancer Progress Report</i> to improve dissemination of data on the cancer burden and progress in cancer control. \$0.50 M 	\$3.5 M
<p>Management and Support</p>	\$2.0 M
Total	\$47.3 M

of the relationship between screening practices and breast cancer mortality, includes data on nearly three million screening mammograms. Key expansion activities include: tracking digital mammography performance as it enters clinical practice, obtaining more detailed risk factor data, and expanding the diversity of the populations represented in the BCSC. Plans for establishing a **Colorectal Cancer Surveillance Consortium** are underway.

The **SEER-Medicare linked data** (www-dccps.ims.nci.nih.gov/ARP/seermedicare.html) is a collaborative NCI/Health Care Financing Administration (HCFA) effort initiated in 1987 to link clinical data collected by the SEER registries with claims for health services collected by Medicare. SEER-Medicare data are being used for a broad array of studies, including those assessing patterns of care, costs of cancer treatment, and use of screening technologies. The data are recognized as a major national research resource for examining dissemination and quality of cancer care. Building on ten years of data from **SEER-based studies**, NCI is now analyzing, presenting, and publishing data on trends in cancer care. An example is the publication of data from the **Prostate Cancer Outcomes Study (PCOS)**, the first longitudinal study on the quality of life of men living with prostate cancer (www-dccps.ims.nci.nih.gov/ARP/PCOS). These data, drawn from a cohort of 3,600 men, reveal significant differences in urinary, bowel, and sexual function over time and between different types of prostate cancer treatment. They will provide patients and their physicians a much better sense of patient-centered outcomes following prostate cancer treatment – a critical element for informed clinical decision making. A major new NCI initiative, **Cancer Care Outcomes Research and Surveillance** (CanCORS), will build on PCOS, supporting research to determine the relationship between various measures of quality of care to important cancer outcomes in patients with lung and colorectal cancer.

NCI is working to improve its understanding of how physicians in the community translate and apply new knowledge about cancer risk, screening, and treatment in the clinical setting (www-dccps.ims.nci.nih.gov/ARP/physician.html). For example, current colorectal cancer screening rates are much too low to have a large impact on col-

orectal cancer mortality. The **Survey of Colorectal Cancer Screening Practices in Health Care Organizations** is assessing current, nationally representative data on the physician and health system factors that may influence the use of screening and diagnostic follow-up for colorectal cancer detection. In the **Physician Survey on Cancer Susceptibility Testing**, national data are being collected on physicians' knowledge of available tests for specific cancer susceptibility genes and on their attitudes toward genetic testing.

While the Cancer Atlas shows differences in the geographic patterns of cancer by disease site and over time, **Geographic Information Systems (GIS)** provide new tools for exploring such patterns and generating hypotheses for etiologic research. In 1999, NCI funded a prototype GIS system for breast cancer research that was piloted as part of the Long Island Breast Cancer Study, applying this emerging technology to the study of possible environmental causes of breast cancer. Through a new initiative, NCI will support research aimed at moving the use of GIS beyond database storage and mapping to become an analytic tool for cancer research.

NCI is supporting a program called the **Cancer Intervention and Surveillance Modeling Network**, the goals of which are to answer the “why” questions in the analysis of cancer incidence and mortality; determine if recommended interventions are having their expected population impact; predict the impact of new interventions on national trends; and study optimal cancer control strategies. In Fiscal Year 2000, nine projects were funded, seven in breast cancer and one each in colorectal and prostate cancer.

A number of national efforts are ongoing in cancer control surveillance. NCI has worked for many years with other Federal agencies, such as the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration, and HCFA to expand the Nation's capacity to track cancer control progress and provide data resources for exploring new leads in cancer etiology. In February 2000, NCI and CDC, established a Memorandum of Understanding to collaborate in **forming a comprehensive, federally integrated cancer surveillance and cancer control research system**.

For more information on SEER, go to www-seer.cancer.gov.

Quality of Cancer Care

THE CHALLENGE

About nine million Americans living today have had a diagnosis of cancer, and another 1.2 million people will be diagnosed in 2000. Of these, a large percentage are undergoing active treatment for their disease, and all require life-long quality care to detect and treat recurrences, new cancers, and treatment side effects, as well as to meet their supportive care needs. This year, direct medical care costs attributable to cancer will exceed \$50 billion. The toll in human pain, suffering, and fear cannot be captured in dollars, but will be keenly felt by the millions of people with cancer, their families, and community caregivers. The National Cancer Institute, long at the forefront of basic and clinical research on cancer and the translation of findings into more effective interventions, is now launching research to improve the quality of cancer care by strengthening the information base for cancer care decision making.

NCI will seek to better understand what constitutes *quality* cancer care, with an emphasis on the patient's perspective; to identify geographic, racial/ethnic, and other disparities in who receives quality care; and to strengthen the scientific basis for selecting appropriate interventions along the entire continuum of care. All decision makers, public and private, will benefit from this expanded information base. Special emphasis will be placed on ensuring that Federal agencies that pay for, directly deliver, or regulate cancer care have the information they need to make quality-enhancing policy choices.

The quality of cancer care is a major national concern that has been underscored by *Ensuring the Quality of Cancer Care*, the report from the Institute of Medicine's National Cancer Policy Board; the 1999 report of the President's Cancer Panel on can-

cer care quality; and initiatives undertaken recently by a number of organizations (e.g., the American Society of Clinical Oncology). These various analyses and proposals for change all point to an emerging consensus about the critical elements of a research agenda to improve the quality of cancer care.

First, we need *a core set of cancer care measures* that are patient-centered and acceptable to providers and payers, span the continuum of care, and meet the highest technical standards of validity, reliability, and sensitivity to change. These end-point measures will greatly enhance our ability to compare interventions across studies and over time.

Equally important, we need a comprehensive, critical evaluation of existing practice guidelines to develop a baseline understanding of what providers and payers currently consider to be "quality" cancer care.

Second, we need a *stronger data and methods "infrastructure" for conducting quality of care analyses*. This includes studies to determine which interventions improve patient-valued outcomes (thereby enhancing the quality of care); to identify geographic or racial/ethnic variations in receipt of

quality care; and to monitor quality over time, at both the individual and population levels. Indeed, the National Cancer Policy Board has recommended the development of a national cancer data system to support such studies on an ongoing basis. Developing this system will require close cooperation among a number of public and private entities, including community- and hospital-based tumor registries, professional associations, and advocacy groups. Such collaboration among public agencies, physician groups, and private organizations that also are working on quality of care initiatives will be essential to improve both the community representativeness of the data and the rigor and relevance of the analyses.

G O A L

Enhance the state of the science on the quality of cancer care and inform Federal decision making on care delivery, coverage, and regulation.

Third, it is critically important to *determine whether therapies shown to be efficacious in clinical trials have been incorporated successfully into community practice*. If so, what were the key factors that made it happen? If not, what explains the failure to turn good science into good medicine? In addition, there should be a critical examination of whether, when, and how NCI-sponsored trials, which have been the backbone of the clinical discovery process in cancer, should give greater emphasis to patient-centered outcomes in addition to the important traditional endpoints of survival and tumor progression.

Finally, the *quality of cancer communications* – for example, between patient and provider, the news media and the patient, and the patient’s family and the third-party payer – is a central determinant of cancer care quality. We must have a better understanding of the information needs of patients, families, and other decision makers involved in the choice of cancer interventions. Based on that understanding, we must develop practical toolkits and other innovative approaches to enhancing access to information relevant to cancer care choices.

This program of research responds directly to the challenges posed in this emerging consensus about how to improve the quality of cancer care. In presenting an initial design of the research program to Department of Health and Human Services Secretary Donna Shalala, NCI urged that cancer be made a “working model” for quality of care research *and* application. The Secretary responded by approving the creation of the Quality of Cancer Care Committee (QCCC), a trans-agency task force with representatives from Federal agencies involved in cancer care delivery (e.g., the Department of Veterans Affairs), coverage (e.g., the Health Care Financing Administration), and regulation (e.g. the Food and Drug Administration). In addition, the NCI quality of care initiative now operates organizationally within the Secretary’s larger Quality Improvement Initiative, in close coordination with the Agency for Healthcare Research and Quality. In all of these efforts, NCI will draw on its experience in supporting, and participating directly in, a number of quality-related projects over the past decade.

NCI understands the importance of ensuring that scientific advances in preventing, detecting, treating, and curing cancer are translated into interventions that extend and improve quality of life for the millions of individuals and families who not only bear the burden but carry the hope. For this to occur, sustained collaboration will be essential not only among Federal researchers and policy makers, but among public agencies and the full spectrum of private entities involved in cancer care – providers and third-party payers, professional associations, patient advocacy groups, and organizations that measure and monitor quality of care. NCI’s quality initiative will be an important early step in support of such sustained collaboration. Moreover, while this research program is clearly cancer-focused, it should deepen our understanding of how to define, monitor, and improve the quality of health care overall.

PROGRESS TOWARD MEETING THE CHALLENGE

NCI’s research programs are providing much of the evidence base for the national agenda to improve health care quality. **The Cancer Care Outcomes Research and Surveillance Consortium (CanCORS)**, launched in 1999, is a major initiative to study the impact of cutting-edge interventions on patient-centered outcomes, investigate the dissemination of state-of-the-science therapies into community practice, and analyze disparities in the delivery of quality cancer care. CanCORS multi-center teams will collaborate on large observational cohort studies of newly diagnosed cancer patients. Initial projects are focusing on lung and colorectal cancer, although expansion to other high-prevalence cancer sites is anticipated. These analyses will support development of an expanded set of core quality and outcome measures that may be collected routinely by tumor registries in support of a national data system to monitor cancer care quality. CanCORS teams also are examining major methodological issues in outcomes research conducted in community settings.

Because results from clinical trials are critical to defining quality cancer care, we are working to ensure the optimal performance of these studies. For example, NCI's Cancer Therapy Evaluation Program is collaborating with the Outcomes Research Branch (see below) in evaluating the **Cancer Trials Support Unit**, a new administrative mechanism for streamlining trials-related data collection and other administrative functions. Part of this evaluation will assess efforts to strengthen the quality of communications about clinical trials to patients and physicians. In addition, the cancerTrials Web site highlights important clinical trials results, providing accurate and timely information to both patients and health care providers.

NCI has long had in place the programmatic and organizational mechanisms to pursue important research questions related to quality of care. Since 1973, the **Surveillance, Epidemiology, and End Results (SEER) program** (www-seer.cancer.gov) has monitored the national cancer burden and provided an indispensable data resource for assessing the impact of research advances on cancer outcomes. For example, **SEER patterns-of-care studies** have shown that, between 1987 and 1995, breast-conserving surgery for early stage breast cancer increased among women of all ages, but that older women were less likely to receive the recommended post-surgical radiation therapy. **Studies linking SEER and Medicare data** have shown that for patients with early stage lung cancer, rates of surgery and survival were lower for black patients than for white patients. The **Prostate Cancer Outcomes Study**, initiated in 1994, is using data from six SEER registries to conduct the first systematic evaluation of the impact of treatments for primary prostate cancer on quality of life for men living with this disease (www-dccps.ims.nci.nih.gov/ARP/PCOS/index.html).

NCI's **Applied Research Program (ARP)** (www-dccps.ims.nci.nih.gov/ARP/index.html) is an established locus of key NCI research on quality issues. In addition to its involvement in the SEER-related efforts described above, the ARP recently launched the **HMO Cancer Research Network**

(www-dccps.ims.nci.nih.gov/ARP/hmo.html), which promotes collaborative cancer research among managed care systems. Supported by the first award under this program, a consortium of researchers affiliated with 10 major not-for-profit HMOs is conducting studies of late stage breast and invasive cervical cancer cases to identify patient, provider, and system factors that could have prevented advanced disease. They also will study the quality and impact of smoking cessation programs delivered in HMOs. To provide a focal point for this emerging research area, in 1999, NCI established an **Outcomes Research Branch** within the ARP (www-dccps.ims.nci.nih.gov/ARP/outcomes.html).

Other NCI quality of care initiatives include the **Breast Cancer Surveillance Consortium**, which examines the accuracy, cost, and quality of screening mammography programs in eight community settings; the newly developed **Colorectal Cancer Surveillance Consortium**; and the **Black-White Cancer Survival Study**.

Budget Increase Request for 2002 Quality of Cancer Care

1. Develop core process and outcome measures for assessing the quality of cancer care.	\$ 1.0 M
2. Strengthen the methodological and empirical foundations of quality of care assessment in cancer.	15.0 M
3. Enhance quality of care research within the restructured NCI clinical trials program.	2.0 M
4. Improve the quality of cancer care by strengthening the quality of cancer communications.	1.0 M
5. Ensure that Federal decision making on cancer care is informed by the best available scientific evidence about quality.	2.0 M
Management and Support	0.5 M
Total	\$21.5 M

THE PLAN – QUALITY OF CANCER CARE

Goal

Enhance the state of the science for defining, monitoring, and improving the quality of cancer care and inform Federal-level decision making on cancer care delivery, coverage, and regulation.

Objectives and Milestones for Fiscal Year 2002

- 1. Develop core process and outcome measures for assessing the quality of cancer care.** **\$1.0 M**
 - Establish a national panel of experts in cancer outcomes measurement theory and practice to evaluate existing endpoint measures and instrumentation and formulate alternative strategies for valid, reliable, sensitive, and feasible clinical and patient-centered endpoint measures for use in quality of cancer care studies. \$0.50M
 - Evaluate published practice guidelines and care maps from major professional organizations, medical care providers, third-party payers, and researchers that describe “quality” cancer care for the most prevalent cancers and across the full continuum of care. \$0.50 M

- 2. Strengthen the methodological and empirical foundations of quality of cancer care assessment.** **\$15.0 M**
 - Sustain support for CanCORS studies of the impact of targeted interventions on patient-centered outcomes, dissemination of state-of-the-science therapies into community practice, the influence of modifiable risk factors, and disparities in the delivery of quality cancer care. \$8.00 M
 - Increase support for analyses of the linked SEER-Medicare database to investigate the diffusion and outcomes of selected cancer interventions, with special emphasis on whether differential application of interventions contributes to cancer outcome disparities among individuals aged 65 and older. \$1.00 M
 - Support the creation of databases that link tumor registry information with private payer administrative data to expand capacity to investigate whether cancer interventions are reaching and improving the health of individuals under age 65. \$2.00 M
 - Sponsor innovative economic and health services research studies on the impact of cancer prevention, control, and screening interventions on patient-valued outcomes and economic costs of cancer to improve cost-effectiveness and outcomes analysis in cancer prevention and screening trials and in community cancer prevention and control interventions. \$2.50 M
 - Sponsor new investigator-initiated studies to strengthen the methodological foundations of outcomes research and quality of care assessment. \$1.50 M

- 3. Enhance quality of care research within the restructured NCI clinical trials program.** **\$2.0 M**
 - Sponsor a symposium and follow-on workshops to bring together leading researchers, patient advocates, and the relevant Federal agencies to assess the current state of the art, identify key research questions, and develop a decision strategy for encouraging comprehensive assessments of patient outcomes in clinical trials. \$0.30 M

- Expand support for studies of diffusion patterns and the overall diffusion rates of important clinical trial findings into community practice. Focus on factors that accelerate or impede the use of new therapies and geographic or population group differences in their availability or adoption. Building on study findings, develop a process for incorporating successful diffusion techniques into clinical trials design and communicating trial results to the public and medical community. \$1.70 M

4. Improve the quality of cancer care by strengthening the quality of cancer communications. \$1.0 M

- Gather nationally representative data to assess the current status of cancer communications and better understand the amount and quality of information now available and being used in cancer care decision making. (See [p. 92](#), Objective 1.)
- Within the Centers for Excellence in Cancer Communications Research, support projects to evaluate and enhance cancer communications' effectiveness in helping patients understand the risks and benefits of interventions and in improving overall quality of care. (See [p. 92](#), Objective 2.)
- Provide supplemental funding to Community Clinical Oncology Programs for pilot projects to identify information needs of cancer patients, survivors, and their families and develop new communications strategies to improve cancer care decision making, particularly in vulnerable populations. \$1.00 M
- Create new communications products and tools for cancer patients and their caregivers, individuals at elevated risk, advocacy groups, health care professionals, third-party payers, and public agencies to improve the accuracy, clarity, and timeliness of cancer care decision making. (See [pp. 92-93](#), Objective 3.)

5. Ensure that Federal decision making on cancer care is informed by the best available scientific evidence about quality measures and assessment. Share new knowledge on ways to translate research into practice at the Federal level with private partners through the National Cancer Policy Board, private associations, and health care systems. \$2.0 M

- To identify and meet Federal agency needs for cancer care information, continue to convene the QCCC. Support and participate in interagency collaborative demonstration projects on quality measures and assessment. \$2.00 M

Management and Support \$0.5 M

Total \$21.5 M

Reducing Cancer-Related Health Disparities

THE CHALLENGE

Despite progress in biomedical science over the past several decades that has increased longevity and improved quality of life for many Americans, the burden of disease is not borne equally by all population groups in the United States. For example, the death rate from prostate cancer among African American men is almost twice that of white men, and stomach cancer mortality is substantially higher among Asian-Pacific Islanders, including Native Hawaiians, than other populations. Cervical cancer incidence in Hispanic women has been consistently higher at all ages than for other women, and African American women have the highest death rate from cervical cancer. Persons of low socioeconomic status have higher death rates for most cancers than persons of higher socioeconomic status. Overall, men are about 50 percent more likely than women to die from cancer, and among all women, Alaskan Natives are about 30 percent more likely to die from cancer.

Disease always occurs within a context of human life circumstances. Social position, economic status, culture, and environment are critical determinants of who is born healthy, who grows up healthy, who sustains health throughout their life span, who survives disease, and who maintains a good quality of life after diagnosis and treatment. In particular, social injustice has to a large extent created the health disparities that currently exist in the United States. **The unequal burden of disease in our society is a challenge to science and a moral and ethical dilemma for our Nation.**

If we are to reduce these disparities, the relative importance of social causes to their development and their relation to factors that result in unequal access to high quality cancer diagnosis and treatment must be explained. To do this, we must increase fundamental research into the social causes of

health disparities, the psychosocial factors that mediate them, and the biologic pathways that can explain their impact.

The relative importance of different determinants also can be expected to vary depending where in the disease process a disparity occurs. A key question is: How can we best measure and monitor cancer-related health disparities across the spectrum of cancer incidence, stage of disease at diagnosis, disease recurrence, quality of life, and cancer mortality? Another key question is the extent to which prevention, early detection, treatment, and communication interventions can effectively reduce cancer-related health disparities.

The National Cancer Institute is strongly committed to a research program that will address cancer health disparities across the cancer control continuum from prevention to end of life care, consistent with recommendations in the Institute of Medicine's report, *The Unequal Burden of Cancer*, and reflected in the Healthy People 2010 goal to eliminate racial and ethnic health disparities.

NCI has developed and will pursue a research framework that builds upon the growing evidence that socioeconomic, cultural, health care provider, institutional, and environmental factors contribute substantially to cancer-related health disparities. The elements that influence health disparities are complex, and their interactions are largely unknown. While health disparities have been framed historically in the context of racial and ethnic disease differences, racial and ethnic classifications have always been socially and politically determined with no basis in biological science. The power of scientific discovery must be used to elucidate the meaning and effect of the human circumstances in which differential disease burdens occur.

Finally, in our national effort against cancer, there is a critical disconnect between scientific discovery and cancer care delivery, and this disconnect

GOAL

Understand the causes of cancer health disparities and develop effective interventions to reduce them.

is itself a key determinant of the unequal burden of cancer in our society. **Barriers that prevent the benefits of research from reaching all populations, particularly those who bear the greatest disease burden, must be identified and removed.** In response to this challenge, we will develop new intergovernmental and public/private partnerships to improve the dissemination and diffusion of evidence-based interventions and encourage the development of health care policies for underserved communities.

PROGRESS TOWARD MEETING THE CHALLENGE

To direct implementation of NCI's **Strategic Plan to Reduce Health Disparities** (ospr.nci.nih.gov/healthdisprpt.pdf) and provide an organizational locus for critical tasks in translating discovery into delivery, NCI has created a **Center to Reduce Cancer Health Disparities**. NCI also has established a variety of infrastructures and initiatives to improve understanding of disparities and develop strategies and interventions to overcome them. These activities provide a firm foundation from which to expand and intensify our efforts.

For example, NCI's **SEER cancer registry program** (www-seer.cancer.gov) has been expanded to cover more of the racial, ethnic, and socioeconomic diversity of the United States, allowing for better description and tracking of trends in health disparities. Methodologic studies are seeking better ways to measure socioeconomic factors and determine their relationship to cancer incidence, survival, and mortality. In addition, NCI supports a growing body of research to examine the environmental, sociocultural, behavioral, and genetic causes of cancer in different populations and apply these discoveries through interventions in clinical and community settings. These interventions cover topics such as tobacco control, dietary modification, and adherence to screening practices. Recognizing the broad relevance of this research to other disease outcomes, NCI collaborates with other Federal agencies in supporting important research initiatives, including co-funded research with the Agency for Healthcare Research and Quality (AHRQ) under its initiative, "Understanding and Eliminating Minority Health Disparities."

NCI's **Office of Special Populations Research (OSPR)** has been a focal point for leadership and coordination on research addressing the cancer-related concerns of underserved and other vulnerable populations. OSPR administers a variety of outreach and other programs targeting specific special populations (ospr.nci.nih.gov). Its newest initiative is the **Special Populations Networks for Cancer Awareness Research and Training (SPN)**, a network of 17 institutions that will create and implement cancer control, prevention, research, and training programs in minority and underserved communities.

The **Comprehensive Minority Biomedical Program (CMBP)** aims to increase the number of minority scientists in biomedical research and enhance the careers of those already in the field. CMBP programs include NCI's newest training initiative for underserved minorities, the **Continuing Umbrella of Research Experiences (CURE)**, and a host of other training opportunities targeting high school students through established researchers. Increasing the representation of ethnic and minority individuals in research and clinical care is crucial to ensure that important research questions about disparities are investigated and that discoveries are translated into community practice. (See [p. 57](#) for a more detailed description of NCI training initiatives targeting special populations.)

Greater participation of minority health professionals in clinical trials is essential to our efforts to explore research questions about cancer-related

Budget Increase Request for 2002 Reducing Cancer-Related Health Disparities

1. Create a plan to organize, coordinate, and monitor NCI activities in health disparities.	\$ 2.0 M
2. Improve capacity and accelerate knowledge through research.	12.0 M
3. Expand our ability to define and monitor health disparities.	9.0 M
4. Expand control intervention research.	17.5 M
5. Expand the channels for research dissemination and diffusion.	7.0 M
6. Strengthen training and education in health disparities research.	1.6 M
Management and Support	1.5 M
Total	\$50.6 M

THE PLAN – REDUCING CANCER-RELATED HEALTH DISPARITIES

Goal

Understand the causes of health disparities in cancer and develop effective interventions aimed at reducing these disparities.

Objectives and Milestones for Fiscal Year 2002

- 1. Create a new and comprehensive plan to organize, coordinate, and monitor NCI activities in health disparities research, education, training, and health services support.** **\$2.0 M**
 - Maintain support for the NCI Center to Reduce Cancer Health Disparities (CRCHD). \$1.50 M
 - Refine and implement an agenda for reducing health disparities. Identify and support successful research activities, facilitate dissemination, and monitor success. \$0.50 M
 - Develop an integrated low literacy education program.

- 2. Improve capacity and accelerate knowledge through fundamental cancer control and population research.** **\$12.0 M**
 - Create 4 Centers for Population Health to (1) expand understanding of the social and environmental causes of cancer-related health disparities and the psychosocial, behavioral, and biological factors that mediate them, (2) develop hypotheses for cancer control research at individual, social, institutional, and policy levels, and (3) develop, apply, evaluate, and disseminate interventions to improve cancer outcomes and reduce outcome disparities. \$8.00 M
 - Expand ongoing epidemiologic investigations to explore racial/ethnic cancer disparities with a focus on cancers for which these disparities are greatest (e.g., breast, cervix, kidney, prostate). Conduct new methodologic studies to evaluate factors influencing recruitment and participation of underserved populations in cancer epidemiology studies. \$4.00 M

- 3. Expand our ability to define and monitor cancer-related health disparities.** **\$9.0 M**
 - Support 2 to 5 new SEER registries to improve coverage of key populations: non-Mexican Hispanics, residents of Appalachia and other rural areas (especially those of lower socioeconomic classes), rural African Americans, American Indians, and populations with high cancer mortality rates. (See [p. 40, Objective 1.](#))
 - Enhance national and regional data systems to measure disparities in cancer-related health behaviors and screening practices. Expand support for supplements to national and regional surveys to enhance data on socioeconomic and other demographic factors associated with disparate cancer outcomes. (See [p. 40, Objective 2.](#))
 - Support statistical and methodological studies to improve accuracy and reliability of data on socioeconomic determinants of cancer rates and risk, health behaviors, and screening in national and regional populations. Expand use of modeling and geographic analyses to examine the unequal burden of cancer. \$9.00 M
 - Conduct national tobacco control surveys on activities that impact tobacco control, including diverse populations. (See [p. 88, Objective 1.](#))

4. Expand cancer control intervention research in prevention, early detection, treatment, and communications. **\$17.5 M**

- Fund an additional 4 to 6 SPN sites to enhance research infrastructure and training in underserved communities. Partner with academic cancer centers to continue developing and testing community-based, participatory cancer control interventions addressing disparities. Provide additional funds for pilot cancer control research projects within SPNs. \$6.00 M
- Provide supplemental funding to Transdisciplinary Tobacco Use Research Centers (TTURCs) to study differential tobacco use and quitting patterns among underserved populations and support development of more effective interventions to reduce the burdens associated with tobacco use. \$1.00 M
- Expand colorectal cancer screening use and follow-up studies. Conduct new intervention research to identify and overcome sociocultural and health care system barriers to the continuing under-use of fecal occult blood testing and flexible sigmoidoscopy, and to address co-morbid illness and other barriers to appropriate clinical follow-up of abnormal findings. \$3.00 M
- Expand research on breast and cervical cancer screening for women who have never been screened and those who are not screened regularly. Support new intervention research to identify barriers to screening for women who underuse or never use breast and cervical screening and address sociocultural determinants in planning, implementing, and evaluating these interventions. \$3.50 M
- Strengthen the methodologic and empirical foundation of quality of care assessment, to improve understanding of unequal access and treatment differences compared to other broader social determinants of these cancer outcomes. (See [p. 46](#), Objective 2.)
- Provide supplements to investigators and cancer centers to expand research on disparities in survivorship, including ethnic, cultural, socioeconomic, and institutional factors affecting the quality and length of cancer survivorship in underserved communities and strategies to help cancer patients and their families make the transition to extended and long-term survivorship. \$2.00 M
- Establish formal affiliations between NCI Cancer Centers and minority-serving institutions. (See [p. 30](#), Objective 1.)
- Provide up to 3 years of supplemental funding to cancer centers to stimulate disparity research, particularly those located in or near underserved communities that experience the heaviest burden of cancer. High priority areas will include disparities in risk factor exposures and access to prevention interventions (e.g., smoking cessation, dietary change, physical activity), quality cancer care, and clinical trials. \$2.00 M

5. Expand the channels for research dissemination and diffusion. **\$7.0 M**

- Work with the Centers for Disease Control and Prevention (CDC) and the American Cancer Society (ACS) to model and monitor the impact of research dissemination and diffusion efforts on DHHS Year 2010 health promotion objectives generally and on cancer-related health disparities in particular. \$1.80 M
- Facilitate adoption of evidence-based cancer control interventions through: collaborative (NCI, CDC, ACS) review of cancer health disparities objectives; consen-

sus on indices of dissemination and diffusion program impact; identification of the most useful formats for presenting intervention research evidence; annual reviews of published evidence on best practices to reduce disparities; and publishing/posting intervention evidence reviews and best practices on NCI's Dynamic Evidence in Cancer Control Web site (dceccps.nci.nih.gov/DECC/default.html). \$2.20 M

- Fund Pilot Projects to Overcome the Digital Divide. (See p. 92, Objective 1.)
- Build special education/dissemination and diffusion partnership programs to reach underserved communities, test these programs' value in reducing health disparities in underserved communities, and make successful pilot programs available for use by local, regional, and national organizations concerned with cancer and public health. \$1.00 M
- Provide one-year competitive supplements to investigator-initiated intervention research grants. Create a supplemental funding mechanism to develop and implement a dissemination and diffusion plan for interventions proven by the original intervention research to be effective in reducing health disparities. \$2.00 M

6. Strengthen training and education in health disparities research.

\$1.6 M

- Develop a new track in the Cancer Prevention Fellowship Program to increase the number of scientists studying health disparities. Recruit 2 fellows per year to focus on health disparities research within OSPR and the Division of Cancer Control and Population Sciences. \$0.50 M
- Expand community-based, cancer control research training within underserved communities. Encourage cancer centers to partner with community organizations and health care institutions in underserved areas to apply for training grant support for community-based clinical and cancer control research training in health disparities research. \$1.10 M
- Expand programs to recruit, train, and sustain underserved racial and ethnic minority individuals in cancer research and provide partnership opportunities for Minority-Serving Institutions with NCI Cancer Centers. (See p. 59, Objective 4.)

Management and Support

\$1.5 M

Total \$50.6 M

health disparities. The **Minority-based Community Clinical Oncology Programs** have for many years sought to address clinical research questions relevant to the disproportionate cancer burden experienced by specific populations. NCI also has established **collaborations with key minority professional organizations** to increase participation of physicians from underserved populations in cancer treatment and prevention trials.

NCI's **Office of Liaison Activities** was established to provide a consistent point of contact with diverse consumer constituencies, to ensure that the

Institute is aware of and responsive to cancer-related issues affecting specific population groups. In addition, NCI has convened a **Special Populations Working Group** to bring to bear the expertise of individuals in the community on the evolving health disparities research agenda.

All of NCI's efforts to explain cancer-related health disparities are closely related to our initiatives to improve the quality of care for people with cancer and those at risk for the disease. (See p. 43 for discussion of our progress in quality of care research and interventions.)

Informatics and Information Flow

THE CHALLENGE

Around the globe, patients and cancer researchers alike are benefiting from the explosive growth of the World Wide Web and advances in computing. But vast amounts of existing knowledge go unused because material from diverse sources cannot be accessed and organized effectively. Therefore, we have asked ourselves, “How can we best collect, manage, and share this information?” To answer this question, NCI is designing a standards-based knowledge management framework – a cancer informatics infrastructure – and a set of tools that will enable us to capture, analyze, apply, and reuse knowledge. This framework will create electronic interfaces among cancer research communities – basic, translational, clinical, and population-based – and with consumers and individuals who deliver cancer care and/or require information. The new framework will unify the research and cancer practice communities by enabling easy access to cancer knowledge, drastically reducing the time and effort needed to generate and use information, and facilitating the rapid translation of research observations into clinical and public health interventions.

As a first step, we are using the cancer informatics infrastructure to increase the speed with which we carry out clinical trials. We have revised our criteria and standards for reporting data collected during a clinical trial and are developing common forms, terminology, and reporting requirements across all types of clinical trials. This uniformity will increase the speed, efficiency, and accuracy of results reporting. Special databases of medical and scientific terminology will help researchers, clinicians, and other users of NCI information systems find and understand the information they seek. NCI's leadership in this area will enable us to estab-

lish a national clinical trials effort that takes full advantage of the information revolution to increase patient accrual, establish common reporting practices, and optimize our ability to share knowledge with the medical and research communities and the public. (Go to cancertrials.nci.nih.gov and select “New Trials System.”)

The new cancer informatics infrastructure is complemented by an NCI program that aims to integrate the informatics elements of the research programs outlined in our extraordinary opportunity areas. An extension of the informatics efforts developed to support the Cancer Genome Anatomy Project (CGAP), this program will provide an essential mechanism to bridge the traditional barriers that block communication of research information among differing scientific disciplines. New integration and tools developed through these efforts will also support the initiatives of the Extraordinary Opportunity for Cancer Communications. The NCI informatics infrastructure will help us address the issue of computer system compatibility, help us manage the burgeoning body of information about fundamen-

tal discoveries, and help alleviate the current bottleneck that exists between discovery and its application. By moving quickly to implement the framework and to develop general tools, we can speed discovery, lower costs for all participants, and capture data electronically in a way that makes information accessible to all participants in the cancer community.

PROGRESS TOWARD MEETING THE CHALLENGE

To reduce the paperwork burden of researchers participating in clinical trials and help them more efficiently develop protocols and test

G O A L
Create an informatics infrastructure that enhances information and resource exchange among researchers, clinicians, and the public.

THE PLAN – INFORMATICS AND INFORMATION FLOW

Goal

Create a cancer informatics infrastructure that enables cancer research by enhancing information and resource exchange among researchers, clinicians, and the public and reduces the barriers experienced by individuals seeking information about cancer prevention, diagnosis, and treatment.

Objectives and Milestones for Fiscal Year 2002

1. **Expand NCI's informatics infrastructure to enable integration and interface within and among basic, clinical, translational, and population research initiatives.** **\$35.3 M**
 - Establish a Center for Bioinformatics that supports the integration of data and tools generated through the NCI's Extraordinary Opportunities and facilitates information exchange within and between NCI-supported research initiatives. \$20.00 M
 - Establish a toolbox of open source informatics applications and services based on a common set of operating principles and standards that support diverse cancer research activities. \$5.00 M
 - Develop research tools that exploit and institutionalize the use of common data elements and a common vocabulary to further the exchange of all types of cancer information and data among the cancer community. \$10.00 M
 - Create a standing review panel for NCI information standards that formalizes NCI's role in the national standards development process and incorporates these standards into the development of informatics research tools. \$0.25 M

2. **Make information on cancer research, diagnosis, treatment, screening, and prevention more readily accessible to the entire cancer community, including physicians, patients, survivors, family members, and persons at risk.** **\$21.0 M**
 - Equip the NCI's cancer information system with powerful facilities for creating, integrating, and accessing a wide range of cancer information resources, including richly formatted and modular text documents and multimedia assets such as images, sound, and video. This technical infrastructure is essential to improve access to relevant and easily understandable cancer information. \$3.00 M
 - Restructure and index current NCI information products, including approximately 300 cancer information summaries and 1,800 ongoing clinical trials descriptions in CancerNet/PDQ. Take full advantage of the NCI's restructured cancer information system to enable all types of users to easily identify and interpret information relevant to their concerns and move seamlessly between different layers of information to find the level most appropriate to their needs. Once complete, users will be able

advances in clinical oncology, NCI is creating the **Clinical Trials Informatics System**. This innovative system links all phases of the clinical trial life cycle, from protocol development, distribution of information to assist patient recruitment, screening, and protocol implementation to publication of clinical trials results. Several components of the system were launched in Fiscal Year 2000, including:

- A document management tool designed to streamline clinical trials' data collection relevant to NCI's scientific, regulatory, administrative, and communication needs. This tool will automate protocol development allowing investigators and NCI staff to concentrate on scientific issues rather than on administrative details. It also will provide administrative information

to identify clinical trials based on specific eligibility criteria. \$7.50 M

- Develop Web-based search tools and user interfaces to extend the NCI's comprehensive electronic cancer information system, making research results and clinical trials information more easily accessible to the public. Extensive cancer vocabulary support will enable creation of both simple and expert search options, including interactive interfaces that guide users to information specific to their needs. \$5.00 M
- Continue evaluating the feasibility of using concept-based searching and natural language processing. Perform pilot tests on existing NCI cancer information systems such as CancerNet/PDQ to ensure that, as the technology advances, NCI is positioned to take advantage of the value these techniques offer. \$1.50 M
- Develop an outreach plan that encourages voluntary electronic submission to CancerNet/PDQ of information about non-NCI sponsored clinical trials, such as trials conducted by pharmaceutical companies and European clinical trials organizations. \$1.00 M
- Modify the processes for writing and reviewing all clinical trials so that development and review can be completed in less than three months. \$3.00 M

3. Make informatics tools easily accessible and use them to integrate and disseminate information from different cancer research communities. \$18.0 M

- Expand the capacity to maintain and distribute an inventory of tools and technologies developed by NCI. \$0.50 M
- Develop an easily accessible and comprehensive electronic clinical trials system to provide uniform and easy access, enhance clinical trials recruitment, and promote scientific knowledge exchange among all participants. \$8.00 M
- Further develop information portals such as the CGAP Web site as broad information access points that provide scientific and clinical information to the research community. \$5.00 M
- Expand systems and tools that facilitate the grant/contract review and award process and simplify management of NCI's cancer research portfolio. \$3.00 M
- Develop and provide methods for non-NCI Web sites and information services to directly search and retrieve information from the NCI's comprehensive cancer information system. \$1.50 M

Management and Support **\$3.0 M**

Total \$77.3 M

for updating and maintaining NCI's clinical trials on the CancerNet Web site.

- A real-time drug inventory developed to reduce drug waste and automate the procurement and distribution of agents used in clinical trials.
- A primary clinical data reporting mechanism for NCI-sponsored trials that will simplify, standardize, and streamline clinical data reporting to

NCI to facilitate drug development and clinical research.

- A system using common data elements, the clinical trial enterprise models, and the CancerNet/PDQ clinical trials registry already in use at NCI to offer oncologists a large portfolio of clinical trials and easy-to-use Web-based patient and enrollment data forms.

- A Web-based clinical trials prototype for electronic submission of clinical trials information to CancerNet/PDQ.

In Fiscal Year 2000, we also created common data elements for breast, lung, and colon cancer treatment trials to help simplify and standardize data collection. In 2001, we will expand our efforts to include treatment trials focused on five additional disease sites as well as prevention, early detection, and screening trials. Through collaboration among all NCI programs involved in informatics activities, we are able to take full advantage of newly developed systems to enhance existing ones.

NCI has made substantial progress in creating a new **XML/SGML-based information infrastructure** to support its comprehensive cancer information products and services, including PDQ and CancerNet. XML-SGML is a non-proprietary standard for storing and managing information. NCI's use of this standard will permit information to be used in a greater variety of information and retrieval environments. A recently developed search and retrieval engine has made possible the much-improved functionality of the redesigned CancerNet Web site. In addition, work is underway to create a powerful new data repository that will permit construction, integration, and maintenance of comprehensive cancer-related information. This new system will support a broad range of content received from a variety of sources, including multimedia assets.

NCI is continuing development of **The Science Place (SP)** (ciiserver2.nci.nih.gov/tsp/index.html), a knowledge management tool created to enable scientists, analysts, and managers to search and retrieve information from many sources, to organize and interrelate it to reflect their personal interests, and to share their information with others. Launched in 2000 after several years of development, the SP enables users to automatically analyze Web-based and other documents for information of interest based on semantic mappings from online vocabulary systems. It also serves as a doorway, or portal, to other NCI tools, such as the Grant Retrieval Information Technology System.

NCI has developed the **Common Scientific Outline (CSO)**, a tool with which we can categorize our research in both a broadly scientific and disease-related manner. By providing the means to

analyze a national/international research portfolio, the CSO can have a profound effect on shaping cancer-related research planning. Using this instrument, NCI and its fellow cancer research funding agencies will have an enhanced foundation for informed discussions and planning.

NCI's award-winning Web-based directory, **NCI Research Resources** (cancer.gov/resources), directs researchers to resources that are generally accessible without extensive negotiation or intellectual property issues and includes descriptions of each resource as well as contact information.

Using the rich and diverse collection of data generated through the various components of the Cancer Genome Anatomy Project (CGAP) (ncbi.nlm.nih.gov/CGAP), NCI has created an **integrated model of cancer-related genomic data** and developed a **Web portal that permits researchers to explore CGAP data** for information such as gene expression patterns in different tissue types or gene variants in the population.

NCI has developed and implemented a **modular computer program that assists in the rapid development, deployment, integration, and maintenance of NCI initiative-specific Web sites**. This program has been used to deploy the prototype Web sites for the CGAP portal, the Mouse Models of Human Cancer Consortium, and the Director's Challenge. In support of the CGAP Web portal, NCI also has developed a prototype for an open source-based informatics architecture that facilitates the retrieval and integration of data distributed among multiple, independent data sources. The open source-based code allows users to modify it at a fundamental level.

Budget Increase Request for 2002 Informatics and Information Flow

1. Expand NCI's informatics infrastructure to enable integration and interface.	\$35.3 M
2. Make information more readily accessible to the entire cancer community.	21.0 M
3. Make informatics tools easily accessible and use them to integrate and disseminate information.	18.0 M
Management and Support	3.0 M
Total	\$77.3 M

Training, Education, and Career Development

THE CHALLENGE

Training, education, and career development for the next generation of scientists remains one of our most important challenges. The scientists of the future will need to be more versatile in their use of new technologies; able to work in teams to understand the complicated environmental, lifestyle, genetic, and molecular variables contributing to human cancers; and better prepared to translate discoveries into public benefit. We need to implement and sustain multiple long-term strategies to attract the most talented individuals to cancer research. We need to create a stable cadre of well-trained technical, biological, behavioral, medical, and public health scientists dedicated to the cancer research enterprise. And we need to ensure that scientists can and will work together effectively to solve problems. Scientists in various disciplines can no longer operate in isolation. The interdisciplinary environment is becoming a way of life for research. Our success will depend upon our ability to move beyond traditional educational and research cultures, overcome health financing constraints, and address socioeconomic inequities that have proven to be barriers to progress in the past. The theme for the future is to train scientists to work on problems as integrated, multidisciplinary teams.

To meet this challenge, we must continue to implement training, education, and career development strategies to address five crucial issues. We must:

- **More adequately prepare basic scientists** by providing them with the background to conduct research directly related to human cancer and preparing them to collaborate with clinical and population scientists and function in team research settings. Ultimately, all of our discoveries in model systems must be confirmed in

human systems, and basic scientists must be prepared to make these critical contributions to cancer research.

- **Reverse the migration of talented and creative physicians from research to practice.** This is the single most threatening consequence to cancer research of the shifting economics of the health care system. We must use more effective ways to train clinical investigators and ensure they have protected time to conduct the patient-oriented research that ultimately will translate basic discoveries into better methods for cancer prevention, diagnosis, and treatment.

- **Increase the numbers and stabilize the careers of cancer prevention, control, population, behavioral, and public health scientists.** The discoveries of scientists dedicated to prevention, early detection, behavior modification, and risk factor analysis will have a major impact on reducing future cancer incidence and mortality. We must develop better ways to train these scientists to function in interdisciplinary research settings and work effectively with patient-oriented and basic scientists. We also must provide them with protected time to do research.

- **Create a research establishment that is ethnically and racially diverse.** We need scientists who are sensitive to the factors that lead to disproportionate cancer incidence and mortality in underserved populations. All scientists must be better trained and prepared to conduct research that will help overcome the cultural and socioeconomic barriers responsible for the unequal burden of cancer.

- **Attract and integrate technical and informatics experts into cancer research.** Specialists in these disciplines are likely to provide a critical driving force for future progress.

G O A L

Prepare a stable, diverse cadre of scientists to work together and use technologies for building knowledge and translating discoveries into application.

THE PLAN – TRAINING, EDUCATION, AND CAREER DEVELOPMENT

Goal

Build a stable, racially and ethnically diverse cadre of basic, clinical, behavioral, and population scientists trained to work together effectively and use the most advanced technologies in building our knowledge base and in translating discoveries into more effective cancer prevention, detection, diagnosis, and treatment strategies.

Objectives and Milestones for Fiscal Year 2002

1. **Continue to provide training, career development opportunities, and protected research time to developing and established cancer scientists.** **\$25.0 M**
 - Maintain a stable NRSA program to train predoctoral and postdoctoral basic scientists through traditional institutional and individual awards. \$3.00 M
 - Continue to increase the participation of clinically trained individuals in basic research and in patient-oriented research by funding 20 new individual mentored awards, 30 new transition awards, and 15 new established investigator awards. \$10.00 M
 - Continue to expand the number of well-trained basic, population, behavioral, and public health scientists in cancer research through the NRSA Program. In addition, fund 20 new mentored awards, 20 transition awards for junior independent scientists, and 10 investigator awards to established scientists. \$7.00
 - Expand the existing NCI Scholars Program by funding 10 additional scholars who will develop their research on the NCI campus and transition to an extramural institution and by initiating 2 new experimental training and career development programs to link the resources of the NCI Intramural Program with extramural institutions. The latter will be used to develop a critical mass of mentors and combined facilities where few institutions have the full range of required capabilities (e.g., prevention, radiation oncology). \$4.00 M
 - Maintain Internet information services that provide full access, descriptions, and instructions for all training and career development opportunities offered by NCI. \$1.00 M

2. **Continue to provide and refine special training and career development opportunities that prepare new and established scientists to function in collaborative, team research settings.** **\$17.0 M**
 - Increase the number of basic scientists conducting human cancer research by funding 30 new special bridging awards that provide both a mentored training experience and transition funding for establishing an independent research program. \$4.00 M
 - Fund 5 new Institutional Clinical Oncology Career Development Programs to prepare clinically trained individuals to become expert in clinical trials design and implementation and lead translational research projects involving teams of clinical investigators and basic scientists. \$3.00 M

<ul style="list-style-type: none"> ■ Implement 10 new Institutional Career Development Programs for cancer prevention, control, population, and behavioral scientists. \$5.00 M ■ Expand and initiate career development opportunities in highly specialized interactive, translational, and research consortia and networks (e.g., Specialized Programs of Research Excellence, Imaging Centers, Tobacco and Tobacco-Related Centers) that are accessible to new and established investigators. \$5.00 M 	\$7.0 M
<p>3. Continue to integrate new technical and research disciplines into the cancer research enterprise.</p> <ul style="list-style-type: none"> ■ Support new specialized institutional education and career development programs that integrate traditional biomedical researchers with other non-traditional sciences (e.g., physics, engineering, informatics) and technology developers. \$6.00 M ■ Support 5 new individual Diversified Sciences Career Development Awards to attract other disciplines into multidisciplinary cancer research settings. \$1.00 M 	\$7.0 M
<p>4. Expand programs to recruit, train, and sustain underserved racial and ethnic minority individuals in cancer research and provide partnership opportunities for Minority-Serving Institutions (MSIs) with NCI Cancer Centers.</p> <ul style="list-style-type: none"> ■ Expand the CURE Program by increasing the number of trainee positions on institutional NSRAs by 50; providing new supplemental funding to 10 cancer centers for high school and undergraduate student research experience; funding 10 new minority training positions in Clinical Oncology Career Development Programs; funding 10 new positions for Cancer Education and Career Development Programs in the population sciences; funding 50 new Minority Investigator Supplements to NCI research project grants; and funding 20 new mentored career development awards for basic scientists and clinically trained scientists. \$11.50 M ■ Develop and add new features to the CURE Program by funding 10 new Career Transition Awards for basic, clinical, and population minority scientists in their first junior faculty positions and 20 NCI Cancer Centers to “broker” connections between minority individuals seeking research experiences and the cancer center scientists. \$2.50 M ■ Expand the number of planning and partnership grants to MSIs and NCI Cancer Centers by funding 10 collaborative planning grants focused on training and education programs, one comprehensive partnership planning grant, and 2 comprehensive partnerships. (See p. 30, Objective 1 for the research aspect of these partnerships.) \$2.00 M ■ Increase minority access to training and career development opportunities by improving NCI Internet information services and linking to public and private agencies that provide related services. \$1.00 M 	\$17.0 M
<p>Management and Support</p>	\$2.0 M
Total	\$68.0 M

PROGRESS TOWARD MEETING THE CHALLENGE

A variety of individual and institutional training and career development awards are being employed to meet the needs of new and established investigators and NCI's anticipated research priorities. Special programs have focused increased resources on career tracks for M.D.s in cancer research, behavioral and population scientists, minority scientists, and scientists in highly technical fields important to the future of cancer research.

Individual Awards

- **Individual mentored five-year awards** provide opportunities for M.D.s in basic or clinical research and individuals pursuing cancer prevention, control, behavioral, and population science.
- **Bridging awards** encourage basic scientists and minority scientists to pursue careers in cancer research. These awards provide a mentored period followed by an unmentored period and protected time for developing first independent research programs.
- **Transition awards** provide for three years of protected time following mentored postdoctoral training or for new investigators to initiate successful research programs. These awards are now in place for NCI's two most critical areas of need, medically trained doctors in basic and clinical research and population scientists. A transition award for minority scientists will be established in 2000.
- **Established investigator awards** provide seasoned investigators in the clinical sciences and in cancer prevention, control, behavioral, and population sciences protected time to conduct research and mentor new scientists. NCI believes that this award for clinical scientists will successfully curtail their migration from research to patient care. This award for cancer prevention, control, behavioral, and population scientists is new in 2000.
- New **diversified sciences career development awards** attract technology developers and scientists in disciplines not traditionally associated with cancer research but clearly needed for the future.

Institutional Awards

Institutional awards are for five years, for developing and conducting training and career development

programs. These awards achieve special goals by establishing specific requirements and assembling mentors whose skills support program objectives.

- **National Research Service Awards (NRSA)**, NCI's mainstay for training basic scientists, now includes provisions for curriculum and research environments that orient all trainees to cancer-related opportunities and approaches of the future.
- **Institutional Clinical Oncology Career Development Programs** prepare the next generation of clinical scientists to design and implement hypothesis-based clinical trials and to collaborate with basic scientists.
- **Institutional Education and Career Development Programs**, initiated in 2000, prepare participants for collaborative, multidisciplinary team research settings.
- The **Continuing Umbrella of Research Experiences (CURE) Program** engages minority high school and undergraduate students and encourages and assists them to become independent investigators.
- **Minority Institution/Cancer Center Partnerships** link over 300 MSIs with NCI Cancer Centers to increase the number of minorities engaged in cancer research; strengthen the research capabilities of minority institutions; and support Centers in reducing cancer incidence and mortality in minority populations.

For more information on these programs and career tracks, go to cancertraining.nci.nih.gov.

Budget Increase Request for 2002 Training, Education, and Career Development

1. Provide training, career opportunities, and protected time for developing and established scientists.	\$25.0 M
2. Provide and refine special opportunities in collaborative, team research settings.	17.0 M
3. Integrate new technical and research disciplines into cancer research.	7.0 M
4. Expand programs for underserved racial and ethnic minorities.	17.0 M
Management and Support	2.0 M
Total	\$68.0 M

People's Story

Ovarian Cancer

My mother died from ovarian cancer when I was 17. By the time she went to the doctor about the leg pains and bloating, the cancer was already advanced.

Symptoms of ovarian cancer are often vague and may be ignored or mistaken for other illnesses. A woman may feel bloated or have general discomfort in the lower abdomen. She may have a loss of appetite or a feeling of fullness, even after a light meal. She also may experience frequent indigestion, gas, or nausea. A tumor that presses on the colon or bladder may cause

diarrhea, constipation, or frequent urination. In some cases, fluid buildup around the lungs can cause shortness of breath. Contrary to common belief, unusual vaginal bleeding is rarely a symptom of ovarian cancer.

This year, an estimated 23,100 new cases of ovarian cancer will be diagnosed in this country, and nearly 14,000 women will lose their lives to the disease. Ovarian cancer is the sixth most common cancer in women, and the fifth most common cause of cancer death among women. It has the highest mortality

rate of all female reproductive system cancers.

We got a computer this year, and I've found information on the Internet about ovarian cancer. The trouble is, there are screening tests, but they're not very effective. It's over 50 miles from our farm to the hospital where the gynecologist is, but I'd make that trip any day of the week for a test that could tell for sure if I have cancer or not.

The lack of a reliable screening test has been a major barrier to improving ovarian cancer detection and decreasing the chance of dying from ovarian cancer. Routine pelvic examination, the standard screening method, misses one-third of even relatively large ovarian tumors. Two other screening tests for ovarian cancer are sometimes used. One is a blood test that measures levels of a protein called CA-125 that is produced by some ovarian cancer cells, and the other is transvaginal ultrasound imaging. However, because both tests have important limitations, they usually are performed only if a woman has symptoms or is known to have an inherited risk for the disease. NCI's Prostate, Lung, Colorectal, and Ovarian (PLCO) Screening Trial (dcp.nci.nih.gov/plco) is currently exploring whether or not routinely using these two tests together might be more accurate and ultimately decrease the number of ovarian cancer deaths.

(continued on next page)



Recognizing the urgent need for better ovarian cancer detection methods, NCI has several exciting new activities underway. Intensive research is being conducted to find more accurate, simple marker tests for ovarian cancer. For example, some studies suggest that ovarian tumors may have unique secretions that, when detected, could signal the earliest stages of cancer, or even pre-cancer. Several centers and laboratories funded under NCI's Early Detection Research Network (edrn.nci.nih.gov) are devoted to identifying such biological indicators of ovarian cancer that could be detected quickly, easily, and accurately.

In addition, because it is so difficult to obtain very early stage ovarian cancer tissue for study, researchers are working on designing mouse models to learn how this cancer develops. Recently, several mouse models for early ovarian tumors have been developed that show promise for uncovering the earliest cellular and related molecular changes that give rise to ovarian cancer. Work in this area has been greatly accelerated by the funding of four Special Programs of Research Excellence (SPoREs) dedicated to ovarian cancer research, and by collaborations among researchers in NCI's Mouse Models of Human Cancers Consortium, *In Vivo* Cellular and Molecular Imaging Centers, Cancer Genetics Network, and the Divisions of Basic Sciences and Clinical Sciences.

There are better treatments for ovarian cancer than there were when my mother was sick, but they still need to be improved.

Following surgery, women with ovarian cancer usually receive a combination chemotherapy that includes a drug containing platinum and a taxane such as paclitaxel (Taxol®). Recurrences may be treated with additional doses of these agents or with other anti-cancer drugs. New or improved treatments for ovarian cancer are being tested in clinical trials. For example, a recently reported randomized trial compared a combination of paclitaxel and cisplatin for treating advanced ovarian cancer with a combination of cyclophosphamide and cisplatin. After nearly four years of follow-up, the paclitaxel/cisplatin patients showed improved survival and remission. Other new therapies under study include high-dose chemotherapy with bone marrow or stem cell transplant, other new chemotherapy combinations, and gene and immune system therapies, such as vaccines that help the immune system recognize cancer cells. In addition, laboratory and animal studies are underway to determine if lowering certain hormone levels in women treated for ovarian cancer will prevent the disease from recurring.

Since my mother had ovarian cancer, my risk for the disease is higher than average. My doctor says that if my mother, sister, or even my daughter has ovarian cancer, I am nearly three times more likely than other women to get it. So I'm going

to be careful – I don't want my kids to lose their mother the way I did.

Five to 10 percent of ovarian cancers are believed to be caused by inherited mutations in the *BRCA 1* or *BRCA 2* genes, which also increase breast cancer risk. NCI is sponsoring further research into inherited genetic ovarian cancer risk through its Cancer Genetics Network, Cooperative Family Registries, and Clinical Epidemiologic Studies in Hereditary Breast/Ovarian Cancer.

NCI is committed to improving ovarian cancer prevention, detection, and treatment, and fully expects that the new ovarian cancer SPoREs, which support innovative, multidisciplinary research with the potential to have an immediate impact on cancer care and prevention, will be important hubs of progress against this disease. In 2001, NCI will bring together leaders in basic, clinical, and population research and the consumer community in a Progress Review Group to assess the state of knowledge and identify research priorities to hasten progress in understanding, preventing, and treating ovarian cancer and other reproductive system cancers in women.

Up-to-date information on ovarian cancer is always available on NCI's Web site, CancerNet (cancer.net.nci.nih.gov) to help women understand this disease and learn about advances in screening, risk assessment, and treatment.

Note: This vignette is a composite of experiences.

Extraordinary Opportunities for Investment

NCI's "extraordinary opportunities for investment" are scientific areas of cancer research in which focused efforts and increased resources can build on past successes to stimulate dramatic progress toward reducing the cancer burden. If pursued, these doors to continued discovery hold great promise to provide profound insights into how cancer develops and to lead to vastly improved techniques for preventing, detecting, diagnosing, and treating various forms of cancer. Although the needed resources are not trivial, our failure to respond quickly with investment in all of these areas will slow the pace of cancer research at all levels and will impair our ability to better care for those whose lives have been touched by cancer.

NCI seeks formal input from a broad spectrum of perspectives from the cancer research community, members of advisory groups, and advocates to identify these areas of exceptional promise. Every three years, we ask these scientific, professional, and lay experts in the cancer field to revisit the "extraordinary opportunities" and select emerging investment

research areas for the next three-year cycle. We assess these responses extensively, blend related ideas, and, with our advisors, select new investment areas. The current set of six extraordinary opportunities were first outlined in NCI's Fiscal Year 2001 budget proposal and are continued in this proposal for Fiscal Year 2002.

To qualify as extraordinary opportunities, research areas must:

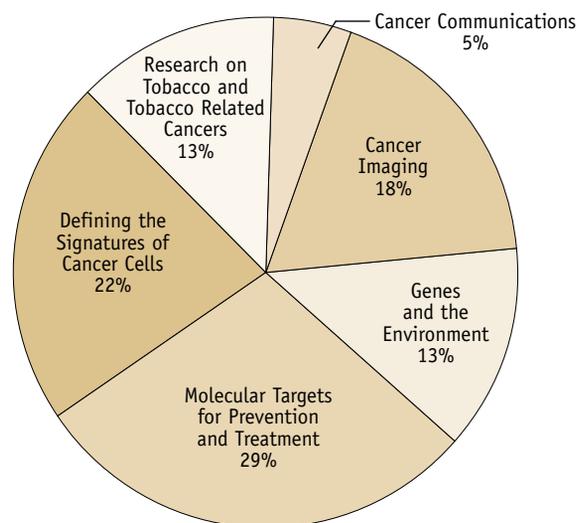
- Respond to important recent developments in knowledge and technology.
- Offer approaches to cancer research beyond the size, scope, and funding of our current research activities.
- Be implemented with specific, defined investments.
- Be described in terms of achievable milestones.
- Promise advances for making progress against all cancers.

These investment areas result in new research awards, new or expanded programs, and collaborations.

Extraordinary Opportunities for Investment Budget Increase Request for 2002

(dollars in thousands)

	Amount
Genes and the Environment	\$68,250
Cancer Imaging	90,550
Defining the Signatures of Cancer Cells	110,750
Molecular Targets for Prevention and Treatment	146,500
Research on Tobacco and Tobacco-Related Cancers	67,000
Cancer Communications	27,500
Total	\$510,550



1

Genes and the Environment

THE OPPORTUNITY

Conceptual and technical breakthroughs and the often breathtaking pace of scientific discovery have engendered among cancer researchers a tremendous sense of optimism that new avenues will be found to prevent, detect, diagnose, and treat cancer. Nowhere is this sense of promise greater or the potential implications more profound than at the interface of epidemiology and genetics. By marrying the study of the distribution and causes of cancer in human populations with cutting-edge genetic and related molecular technologies, we will over time be able to:

- Identify genes that predispose people to cancer and point to previously unsuspected environmental carcinogens.
- Study genetically susceptible subgroups to predict the increased risk that may result from their exposure to certain types of substances in the environment.
- Quantify the cancer risks associated with specific environmental and genetic factors and their interactions, enabling us to guide individual and public health strategies aimed at preventing and controlling cancer.
- Design new approaches to health and cancer care based on an understanding of how genes modify and interact with environmental exposures.

The pivotal role of lifestyle and other environmental exposures as causes of cancer is reflected in the substantial variation in cancer incidence around the world and in the changes in risk observed among groups that migrate and settle in a new country. Furthermore, epidemiologic research has identified a wide range of cancer-causing exposures including tobacco use, dietary components,

sunlight, ionizing radiation, environmental chemicals, and infectious agents as well as risk factors such as obesity, exercise, hormones, reproductive factors, and sedentary lifestyle.

Cancer susceptibility is another critical piece of the puzzle. For example, why does one person with a cancer-causing exposure (smoking or infection with human papillomavirus, for example) develop cancer, while another does not? Intensive study of rare cancer-prone families has provided insights into this apparent paradox. We know that disruption of fundamental cellular processes contributes to the development and progression of the more common, non-hereditary forms of cancer. Yet even among individuals who have inherited cancer-predisposing genes, the risk of developing cancer appears to be modified by other genetic and environmental factors. There is mounting evidence that a person's genetic make-up may influence susceptibility or even resistance to cancer-causing exposures. Opportunities now exist to determine how variations in these genes combine with environmental and other factors to induce cancer in the general population.

The exciting opportunities of this emerging field are accompanied by enormous challenges. Population studies sufficiently powerful to examine the complex interactions of multiple genetic and environmental factors will require unprecedented numbers of participants and will demand new research infrastructures and strategies for interdisciplinary collaboration. As we gain in our understanding of individual-specific risk factors, we must strive to ensure that this knowledge is used appropriately and is not harmful to the individual. Psychosocial, legal, ethical, and clinical issues must be addressed, and individuals, families, and health care providers must be able to take appropriate action without repercussions.

G O A L

Discover genetic, environmental, and lifestyle factors and their interactions that define cancer risk and inform strategies for cancer control.

PROGRESS IN PURSUIT OF OUR GOAL

NCI's earlier investments into the study of genetics have yielded enormous dividends. For example, NCI's Cancer Genome Anatomy Project (CGAP) has resulted in the discovery of over 44,000 new genes. New technologies have permitted scientists to determine which genes are active in normal or in cancerous tissues. There has been an exponential increase in the pace of identifying genes that maintain the integrity of our genetic material, regulate cell growth and development, and determine our response to hormones and other chemicals produced by the body or in the environment. Related discoveries have enabled us to characterize the function of hundreds of new genes and pathways. Vast public databases contain millions of entries describing gene sequences and their location in the human genome.

Establishing significant and valid evidence for gene-environment interactions requires studies of large populations over long periods of time. In *cohort studies*, information on exposures to factors that might affect cancer risk and biologic samples are collected from individuals in large population subgroups. By systematically following these people over time to determine who develops cancer and who remains cancer free, scientists can understand the risk of developing cancer for those with specified exposures and genetic profiles. In this way, early detection can be directed to those at greatest risk and diagnosis and treatment can be tailored to individual needs. NCI is establishing a **Cohort Consortium** of investigators from around the world to facilitate the pooling of data on very large numbers of people, foster collaborative links among resources, and organize collaborative studies. *Case-control studies* retrospectively examine exposure histories and genetic profiles of people who already have cancer (cases) and compare them with those of people who have not developed cancer (controls). NCI is assembling a **Case-Control Consortium** to support large-scale studies of gene-environment interactions for less common cancers.

NCI has expanded the tools available to the cancer genetics community through the World Wide Web. Through the **Genetic Annotation Initiative** (GAI) of CGAP, scientists have identified more than 20,000 genetic variations, and they

expect to expand that number to nearly 500,000 by 2002. Researchers are using sophisticated computer programs to identify variations in specific genes in people with cancer to determine which variants are associated with certain types of cancer and whether some variants occur more often in some populations. New technology development through the **Innovative Molecular Analysis Technologies Program** is also improving our ability to effectively analyze the large volumes of samples and data in these population-based studies.

Members of the **Mouse Models of Human Cancers Consortium** (MMHCC) are developing and validating mouse models – mice with cancers similar to the major human cancers that can be inherited. These models will be made available to scientists for research. Composed of 20 groups of investigators from institutions across the country, the MMHCC uses Web-based discussion forums and other communication tools to integrate emerging knowledge about cancer susceptibility from animal models with studies on human populations. The MMHCC also supports a repository for models of key cancers caused by specific gene variants.

We have gained tremendous insight into risks for cancer by examining the personal and medical histories of high-risk families and investigating how

Budget Increase Request for 2002 Genes and the Environment

1. Identify environmental risk factors and susceptibility genes. Determine their interactions in cancer causation.	\$22.0 M
2. Develop new ways of assessing and measuring environmental exposures.	10.5 M
3. Identify and characterize gene variations.	4.0 M
4. Develop new experimental models.	5.0 M
5. Identify cancer-predisposing genes in high-risk families.	8.0 M
6. Refine cancer risk prediction methods/models.	6.8 M
7. Expand enrollment of genetically high-risk individuals into clinical protocols and conduct cancer susceptibility studies.	9.0 M
Management and Support	3.0 M
Total	\$68.3 M

THE PLAN – GENES AND THE ENVIRONMENT

Goal

Discover genetic, environmental, and lifestyle factors and their interactions that define cancer risk and can inform the development of new strategies for prevention, early detection, and treatment.

Objectives and Milestones for Fiscal Year 2002

- 1. Identify new environmental risk factors and susceptibility genes and determine their interactions in cancer causation. \$22.0 M**
 - Expand the biospecimen collections of the Cohort Consortium to increase the number of individuals and diversity of the populations covered and to allow development of studies of gene expression and other molecular profiles. \$6.00 M
 - Fund and conduct 2 large gene-environment, case-control studies of less frequently occurring cancers, one in a population-based cooperative group and the other in a hospital-based group. Cancer types selected will be based on increased incidence, ethnic disparities, and geographic patterns. \$10.00 M
 - Begin development of 2 regional centers for state-of-the-art biospecimen processing and storage and for high throughput genotyping to support molecular epidemiology and other interdisciplinary studies of human cancer. \$4.00 M
 - Continue development of informatics systems to collect, store, analyze, and integrate the vast amounts of epidemiologic, clinical, and laboratory data. \$2.00M

- 2. Develop new ways to assess and measure environmental exposures for use in population studies. \$10.5 M**
 - Continue developing new epidemiologic methods for assessing complex exposures over a lifetime. Coordinate the use of these methods for gene-environment interaction studies. \$2.00 M
 - Further expand NCI's Innovative Molecular Analysis Technologies Program to develop new non-invasive techniques for collecting and measuring DNA and proteins in very small amounts of biologic material. Apply these techniques to large-scale studies of gene-environment interactions. \$2.00 M
 - Supplement ongoing research programs to develop and validate measures of the cumulative cellular, genetic, and molecular effects of exposure to environmental carcinogens in non-tumor tissue. \$1.00 M
 - Continue to expand and supplement research programs to develop and validate molecular approaches to define mutation patterns that implicate specific carcinogens. \$1.00 M
 - Use emerging technologies to develop molecular and immunologic techniques that will enable screening of large numbers of biologic samples to identify infectious agents relevant to human cancer. \$4.00 M
 - Continue to work with academic centers, cancer centers, and schools of public health to develop model training programs in molecular epidemiology. \$0.50 M

- 3. Identify and characterize gene variations involved in molecular pathways important in cancer. \$4.0 M**
 - Extend CGAP's GAI efforts to identify new gene variants relevant to cancer in clinically- and epidemiologically-defined populations. \$2.00 M

- Expand the GAI's efforts to define key molecular pathways by performing comprehensive genetic variation characterizations on an extended set of gene and protein expression profiles. \$2.00 M

4. Develop new experimental models that parallel human cancer-related genes, pathways, and processes. \$5.0 M

- Augment the MMHCC to:
 - Derive and refine mouse models of human hereditary cancer genes for which models do not exist. \$1.00 M
 - Generate valid mouse models based on epidemiologic observations of genetic and environmental modifiers of cancer risk. \$1.00 M
 - Evaluate within the collection of appropriate models the potential for environmental factors to modify cancer development. \$1.00 M
 - Discover biomarkers and *in vivo* approaches for early detection of cancer and to develop and test new prevention strategies. \$1.00 M
- Stimulate development of new non-mammalian models of complex interactions among the pathways and processes that contribute to cancer etiology. \$1.00 M

5. Identify cancer-predisposing genes in high-risk families and investigate how expression of these genes is modified by other genes and environmental factors. \$8.0 M

- Fund 2 new consortia of investigators to identify the genetic basis of familial aggregations of cancers not currently linked to genes. \$2.00 M
- Expand the network of cooperative registries to enhance recruitment of high-risk families and foster development of shared informatics and other research tools. \$3.00 M
- Initiate large collaborative interdisciplinary studies of high-risk families to quantify cancer risk among carriers of major genes and investigate the genetic and environmental modifiers of risk. \$1.00 M
- Continue to expand the capacity and use of the NIH Center for Inherited Disease Research and other activities to accelerate cancer gene identification. \$1.00 M
- Initiate collection of fresh-frozen tumor tissue and other biospecimens from genetically cancer-prone individuals and families for microarray-based analyses of molecular signatures of cancer. \$1.00 M

6. Refine cancer risk prediction methods/models to integrate genetic and environmental determinants of cancer. \$6.8 M

- Augment clinical trials and observational studies of breast cancer to validate current risk prediction models and formulate new ones. Expand development of risk models that predict the occurrence of other major cancers. \$2.00 M
- Expand risk prediction model application to target interventions aimed at cancer prevention, detection, diagnosis, or treatment. \$1.50 M
- Extend risk models to account for both cancer and non-cancer risks and to fit ethnic and minority populations. \$1.00 M

- Devise and test risk communication strategies best suited to patients, professionals, and policy makers. \$2.00 M
- Create a risk prediction model prototype that accommodates gene-environment interactions for selected cancers. \$0.25 M

7. Expand enrollment of genetically high-risk individuals into clinical protocols and conduct studies to address the clinical, behavioral, and societal issues associated with cancer susceptibility. \$9.0 M

- Recruit genetically high-risk individuals into clinical studies to assess the efficacy of preventive, early detection, diagnostic, and treatment interventions. \$2.50 M
- Continue support for behavioral research within NCI-funded networks and other settings to assess the impact of predictive genetic testing and cancer risk assessment on high-risk individuals and their families and to develop and evaluate interventions that mitigate the negative consequences of genetic testing. \$2.50 M
- Support research in cancer survivorship to enable long-term follow-up of cancer patients on the late physical and psychosocial effects of treatment and to evaluate the role of genetic susceptibility in these outcomes. \$2.50 M
- Continue and expand development and evaluation of educational tools to facilitate informed decision making about participation in cancer genetics research, genetic testing, and cancer risk reduction. \$1.50 M

Management and Support **\$3.0 M**

Total \$68.3 M

cancer-predisposing genes are modified by other genes and environmental factors in these families. For example, through the **Cooperative Family Registries** for breast/ovarian and colorectal cancers, we have collected clinical, epidemiological, and pathological data as well as biospecimens for over 8,000 high-risk families. Analysis of this information may lead to targeted approaches for the prevention, detection, and diagnosis of cancer.

New insights into genetic susceptibility, environmental carcinogens, and their potential interactions can be incorporated into **cancer risk prediction models** that can in turn be used to estimate individual risk. Breast cancer risk models have been employed in two large cancer prevention trials and were found to be good predictors of cancer risk. We now want to develop risk models for other cancers.

Clinical trials involving genetically high-risk individuals can increase our understanding of the clinical, behavioral, and societal issues associated with cancer susceptibility. One project in this area

has been a feasibility study of the comparative value of early screening and diagnostic tools in breast cancer gene mutation carriers. Another study is a pilot program for screening and chemoprevention in men who carry susceptibility genes for breast or ovarian cancer, which have been shown to increase prostate cancer risk. To gain further insights into early detection, NCI has begun a follow-up study of women prone to breast cancer who gave cell samples that were used to search for molecular fingerprints of pre-malignant cells.

NCI has established a **state-of-the-art bioprocessing and biorepository facility and a genotyping facility** to handle large volumes of specimens and data to support NCI efforts in molecular epidemiology. These facilities are prototypes for a regional network to support molecular epidemiology studies.

For more information on NCI's Genes and the Environment initiatives, go to cancer.gov/initiatives.

THE OPPORTUNITY

As recently as 25 years ago, a physician or surgeon who suspected the presence of a tumor in a patient had few options: order x-ray studies to find the tumor's exact location, schedule the patient for surgery, excise a portion of the unhealthy tissue for biopsy, remove the tumor, and explore surrounding tissues to determine if the cancer had spread. Over the last quarter century, imaging technology refinements have substantially broadened the range of medical options. Imaging tests now provide much clearer and more detailed pictures of organs and tissues. New imaging technology allows us to do more than simply view anatomical structures such as bones, organs, and tumors. Functional imaging – the visualization of physiological, cellular, or molecular processes in living tissue – enables us to observe activity such as blood flow, oxygen consumption, or glucose metabolism in real time.

As we understand more fully cancer's fundamental nature, our capacity to use imaging tools to detect the molecular changes associated with a tumor cell promises to vastly improve our ability to detect and stage tumors, select treatments, monitor the effectiveness of a treatment, and determine prognosis.

Detection and Diagnosis

Imaging technology already has had lifesaving effects on our ability to detect cancer early and more accurately diagnose the disease. For example:

- X-ray mammography has revealed the presence of very small cancers in thousands of women before the tumors could be detected by physical examination.
- Computed tomography (CT) and ultrasound permit physicians to guide long, thin needles deep

within the body to biopsy organs, often eliminating the need for an open surgical procedure.

- CT can show if a tumor has invaded vital tissue, grown around blood vessels, or spread to distant organs.

As the science advances, seeing how the processes and pathways inside a cell change as the cell transforms from normal to cancerous will allow us to detect changes in people earlier, and eventually we expect to be able to visualize the actual molecular signatures of a cancer. We will be able to tell, in the radiology suite of a hospital, which genes are being expressed in a patient's cells, and we will be able to translate this information directly into better management of the disease.

G O A L

Accelerate discovery and development of imaging methods that will predict clinical course and response to interventions.

Treatment

In addition to using CT and other imaging technologies to guide treatment choices, combining precise imaging techniques with radiation sources and high performance computing is improving our ability to shape radiation treatments to the tumor's three-dimensional contours. Using today's technology, we can identify the kinds of molecular structures/receptors that cover the surface of a tumor and use this information to predict how it may respond to certain treatments. With a picture of how glucose is being used in tumor cells, we can tell – without the need for a biopsy – how a tumor is responding to a recently administered treatment.

In principle, imaging techniques can be interfaced with other tumor killing approaches – toxic chemicals, gene therapy, heat, and cold – to more precisely guide tissue destruction at the tumor site. Being able to distinguish between cancerous and normal tissue and deliver treatments only to diseased tissues in a minimally invasive way has the potential to minimize surgical trauma, shorten recovery time, and reduce health costs.

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PROGRESS IN PURSUIT OF OUR GOAL

We have made important strides, but much remains to be done before the full promise of the imaging sciences is realized for cancer research and care. Having laid the groundwork, we are working toward greater improvements in cancer detection, diagnosis, and treatment that will provide real benefits for people with cancer and those at risk. Several new initiatives illustrate our progress.

To foster multidisciplinary research on cellular and molecular imaging, NCI has established three **In Vivo Cellular and Molecular Imaging Centers** (ICMIC) and awarded ten planning grants for additional Centers. These Centers will narrow the gap between the discovery of new cancer genes and intracellular pathways and the translation of these discoveries into clinically useful, minimally invasive imaging approaches to expanding our understanding of cancer.

NCI is funding projects to assist investigators and small businesses in developing **digital mammography display and workstation technology**. Digital mammography is one of the most promising technologies for use in large-scale screening programs to improve breast cancer detection.

To speed the development of new imaging methods, NCI has created the **Small Animal Imaging Resource Program** (SAIRP). Our five SAIRP centers are developing and applying a wide variety of functional, quantitative imaging modalities. For example, an SAIRP-developed magnetic resonance (MR) technique can detect prostate tumors less than one millimeter in size in a mouse model. An MR technique that measures the growth of brain tumors in rats is being used to look for very early recurrence of brain tumors in children. Quantitating imaging data for small animals will lead the way to methods that can be applied in humans. The SAIRP's progress in technology development and its usefulness as a resource to cancer researchers, particularly Mouse Models of Human Cancer Consortium (MMHCC) researchers, has been greater than anticipated. NCI's **Preclinical Models Imaging Forum** will link experts in the MMHCC and the SAIRP, and information from the forum will help in developing and validating new preclinical models and in designing

and testing imaging techniques to detect human cancers.

NCI has launched the **Diagnostic Imaging Network** in partnership with the American College of Radiology. The Network brings together imaging experts to perform a broad spectrum of multi-institutional clinical trials on new and refined imaging tools. A number of such trials have been launched or are in preparation, including a comparison of MRI and CT in diagnosing gynecologic cancers, the use of positron emission tomography (PET) to monitor response to chemotherapy, assessment of spiral CT for detecting lung malignancies, a comparative study of digital versus conventional mammography, and a comparison of MRI versus CT for staging pediatric malignancies.

The **Development of Clinical Imaging Drugs and Enhancers** (DCIDE) program will foster and speed the development of promising imaging enhancers (contrast agents) and molecular probes and their translation from laboratory synthesis to Investigational New Drug (IND) application. NCI will make its preclinical development resources available to competitively selected developers of a promising diagnostic agent or probe in order to remove a recognized barrier between laboratory discoveries and their entry into the clinic. To further aid the development of promising imaging agents, NCI is launching a DCIDE-like program to fund early trials of novel imaging probes.

To improve imaging technologies for prostate cancer detection that could enable clinicians to more accurately localize and stage a tumor and select an optimal therapy, NCI has established the **Phased Innovation Award for Diagnostic Imaging and Guided Therapy in Prostate Cancer**. In 2001, several awards will be made for research to improve image-guided surgery and radiotherapy.

The **Innovative Technologies for the Molecular Analysis of Cancer** award provides assistance for high-resolution cellular or molecular imaging research, access to tissue samples, development of preclinical models, and the conduct of clinical investigations as an important extension of molecular analysis methods. The **Applications of Innovative Technologies for the Molecular Analysis of Cancer** awards will provide a means of piloting and evaluating newly developed high-resolution imaging technologies.

To promote the development, testing, and adoption of new imaging modalities and applications, NCI has organized a unique **forum that brings together technology developers from academia and industry with the funding agencies, regulators, and reimbursers of technology**. NCI's partners include the Food and Drug Administration (FDA), the Health Care Financing Administration (HCFA), other third-party payers and providers, and major device manufacturers through the National Electrical Manufacturers' Association. These partnerships promote communication and progress in this critical area. The first forum was held in September 1999 and the second is planned for September 2000.

NCI, FDA, and HCFA also have formed an **Interagency Council on Biomedical Imaging in Oncology** to offer a multi-agency perspective on communicating with government for investigators and manufacturers attempting to bring emerging medical imaging technology to the marketplace. Council members have experience and knowledge about their agency's decision making processes concerning medical imaging products and will provide advice on projects or proposals voluntarily submitted by investigators and technology developers in industry and academia.

Because partnerships are critical in developing new and emerging imaging technologies, NCI has formed a **partnership with the National Science Foundation** (NSF) to stimulate research on biophotonics – the study of light and its clinical applications. In addition, plans have been laid for NSF to fund image processing research using a spiral CT lung database developed through NCI-sponsored research.

NCI also plays a key role in the trans-NIH **Bioengineering Consortium** (BECON – see grants.nih.gov/grants/becon/becon2.htm), which fosters new basic understandings, collaborations, and transdisciplinary initiatives among the biological, medical, physical, engineering, and computational sciences related to bioengineering applica-

tions and advances. Research and collaborations supported through BECON will help NCI develop imaging technologies for detecting and treating cancer.

For example, NIH has created the **Bioengineering Research Partnership Programs** to support multidisciplinary research teams with bioengineering expertise that are applying an integrative, systems approach to developing knowledge or methods to prevent, detect, diagnose, and treat disease and understand health and behavior. NIH also has established the **Bioengineering Research Grants** initiative with a similar scientific scope, but designed for a limited number of investigators or institutions.

For more information on NCI's Cancer Imaging initiatives, go to cancer.gov/bip or cancer.gov/initiatives.

Budget Increase Request for 2002 Cancer Imaging

1. Strengthen the foundations of imaging technologies and methodologies.	\$11.0 M
2. Expand the development of novel imaging agents.	8.1 M
3. Integrate molecular and functional imaging methods into molecular target discovery, drug development, and early clinical trials.	5.0 M
4. Develop and use imaging as an endpoint in clinical trials.	48.5 M
5. Accelerate development and clinical testing of image-guided interventions.	5.0 M
6. Develop and conduct early clinical trials of innovative imaging technologies.	5.0 M
7. Establish information archives and repositories for the research community.	4.5 M
Management and Support	3.5 M
Total	\$90.6 M

THE PLAN — CANCER IMAGING

Goal

Accelerate discovery and development of imaging methods to identify the biological and molecular properties of precancerous or cancerous cells that will predict clinical course and response to interventions.

Objectives and Milestones for Fiscal Year 2002

- 1. Strengthen the foundations of imaging technologies and methodologies to assist in fundamental investigations of cancer.** **\$11.0 M**
 - Fund 2 additional ICMICs. \$4.00 M
 - Fund 8 to 10 supplements for collaborations between SAIRPs and other NCI programs such as the MMHCC. \$3.00 M
 - Fund 8 to 10 seed grants and 6 Phased Innovation Awards for research on clinical applications of optical technologies, or integration of optical technologies with other imaging. \$4.00 M

- 2. Expand the development of novel imaging agents.** **\$8.1 M**
 - Increase the number of imaging agents supported by the DCIDE program from 6 to 12 per year. \$6.00 M
 - Increase contract support for early clinical trials of imaging agents (safety and efficacy studies) from 8 to 12 trials per year. \$2.00 M
 - Enhance the publicly available database of imaging agents by adding information on their properties. \$0.10 M

- 3. Integrate molecular and functional imaging methods into molecular target discovery, drug development, and early clinical trials.** **\$5.0 M**
 - Fund 8 supplements for imaging collaborations with the grantees in the Molecular Target Drug Discovery initiative. \$2.00 M
 - Fund 6 to 8 supplements for developing imaging cores within the Interdisciplinary Research Teams for Molecular Target Assessment. \$2.00 M
 - Fund imaging cores within the Molecular Target Laboratories. \$1.00 M (For more information about molecular target initiatives, see pp. 82-83.)

- 4. Develop and use imaging as an endpoint in clinical trials.** **\$48.5 M**
 - Fund supplements for 10 to 15 imaging cores within NCI-funded Cancer Centers to provide expertise in clinical trials that use imaging results as an endpoint. \$5.00 M
 - Support expert panels to develop consensus criteria for using imaging results as endpoints in clinical trials. \$0.20 M

<ul style="list-style-type: none"> ■ Continue to fund the clinical trial to evaluate the potential clinical benefit of digital mammography compared to conventional mammography. \$9.00 M ■ Continue to fund a randomized pilot study to assess feasibility of conducting a definitive clinical trial of spiral CT as a screening method for lung cancer detection. \$2.00 M ■ Continue to fund a large definitive randomized clinical study of spiral CT as a screening method for lung cancer detection if pilot study shows randomized design to be feasible. \$30.00 M ■ Fund clinical studies to: compare CT colonography with endoscopic colonography for early detection of colon cancer and polyps; evaluate magnetic resonance spectroscopy for early detection and assessment of prostate cancer; and evaluate the role of (F-18) – fluorodeoxyglucose PET studies for staging lung cancer. \$2.25 M 	
5. Accelerate the development and clinical testing of image-guided interventions.	\$5.0 M
<ul style="list-style-type: none"> ■ Fund 6 to 10 Phased Innovation Awards for image-guided therapy research emphasizing a problem-solving, organ-specific approach and promoting interactions between clinicians and bioengineers. \$3.00 M ■ Fund 4 to 6 supplements for collaborations between the Clinical Trials Cooperative Groups and the Diagnostic Imaging Network for testing promising, minimally invasive, image-guided interventions. \$2.00 M 	
6. Develop innovative imaging technologies and conduct early clinical trials of new devices.	\$5.0 M
<ul style="list-style-type: none"> ■ Create a competitive program in which innovative equipment prototypes developed in industry and academia are provided to selected academic institutions for feasibility testing, in collaboration with the developer. \$5.00 M 	
7. Establish information archives and repositories for the research community.	\$4.5 M
<ul style="list-style-type: none"> ■ Establish data banks of standardized digital image data associated with known clinical outcomes to provide a research resource for investigators. \$2.50 M ■ Fund 6 to 8 grants to develop and test image processing and analysis algorithms using these standardized data sets. \$2.00 M 	
Management and Support	\$3.5 M
Total	\$90.6 M

3

Defining the Signatures of Cancer Cells: Detection, Diagnosis, and Therapy

THE OPPORTUNITY

In the 19th century, the light microscope opened a new frontier in the study of disease by opening a window on the inner workings of the cell. With this instrument, pathology – the branch of medicine that deals with the essential nature of disease – expanded to include the study of structural changes in cells. For the first time, disease could be linked to visible, recognizable changes in cells of the body.

At the cusp of the 21st century, new molecular-based technologies are bringing us to a similar revelation. These new technologies are enabling us to identify features of individual cells in ways unimagined by our 19th century predecessors. For example, all cell types, depending on their functions, have unique, identifiable “signatures” or special characteristics, such as which genes are active and what proteins or other cellular products are manufactured by the cell. Our new technologies are enabling us to read and understand those signatures.

We have learned that during the transformation of a normal cell to a cancer cell, the signature changes, and that change becomes a signal of the presence of cancer. Further, we have learned that cells surrounding an incipient tumor may also undergo changes, indicating that cancer is present. For example, tobacco-induced molecular changes in the mouth may predict the risk of developing lung cancer, and cancers of the urinary tract may be signaled by cancer cells that are “shed” in the urine. Reading the signatures of these easily accessed cells may enable us to develop simple, non-invasive tests to find cancers located deep within the body.

The implications of these findings are profound. By reading cellular signatures accurately, we may be able to detect and diagnose cancers before they

have had a chance to invade nearby tissues. In fact, with the tools we are developing, a single drop of blood from a patient’s finger may be all that is needed to find a cancer, assess the threat it poses by comparing its traits to profiles in an online library of tumor characteristics, choose the best possible treatment, and monitor the patient’s recovery. By assessing the meaning of individual changes in the cell’s signature, we may be able to determine which cancers are most likely to progress and which are less likely to do so. This will be especially valuable to doctors and patients, such as those with prostate cancer, who are sometimes confronted with hard decisions and a desire to avoid the consequences of unnecessary treatment. By studying the sequence of changes a cell undergoes as it transforms from normal to cancerous, we will gain important insights into the etiology of the disease. By applying what we have learned, we will be able to identify new targets, at the molecular level, for effective prevention and treatment.

“Defining the Signatures of Cancer Cells” was first identified as an area of extraordinary scientific opportunity in 1996, and it continues to be an area

rich in scientific promise today. For example, we now are in a position to learn new ways to characterize tumors more efficiently – that is, to determine which genes are active and inactive, and the levels of specific proteins that are present in a particular tumor. Such “molecular fingerprinting” will markedly improve the specificity of cancer diagnosis by allowing us to differentiate among tumors at the molecular level, and should enable us to devise treatments targeted at cellular subtypes of different cancers. See *Molecular Targets Extraordinary Opportunity*, p. 80. We now can use changes in molecular signatures to help us identify infectious and environmental agents that may be responsible

G O A L

Generate a catalog of distinguishing molecular signatures of cells to develop new diagnostic and therapeutic approaches and predict response.

for the development or progression of a tumor. In addition, while many of our previous efforts have centered on identifying genes involved in cancer, we are very interested in learning more about the cellular functions of the proteins produced by these genes. Finally, there has been a gap among the identification of preclinical tumor changes, early evaluation of new identification techniques, and their clinical application. We now have the opportunity to synthesize these disparate findings into a body of knowledge that will translate into real health benefits. Our ultimate goal is to push back the detection and diagnosis of cancer to the earliest stages, thereby offering the potential to focus intervention efforts at preventing overt disease.

Clearly, we have made substantial progress, but much remains to be done if we are to take full advantage of the opportunities in this area. Identifying the molecular signatures of cancer is drawing a valuable, though static, picture of the molecular composition of a cancer cell, providing an opportunity to begin to develop targeted diagnostics and therapeutics. However, a full understanding of cancer initiation and progression will require a dynamic understanding of the process. Thus it is important to understand how alterations in a few molecules might affect a variety of cellular functions. To achieve this understanding, we need to assemble the molecular signatures information into a complete picture of the living cancer cell. In addition, the diagnostic value of molecular-based methods must be confirmed and their practical benefits established against the background of conventional medicine. New technologies must be developed, and new preclinical models must be created and validated to establish our findings. Finally, to validate the predictive value of the new approaches, we must develop the sophisticated computer systems, databases, and statistical methods needed to integrate the complex information being generated by these new technologies with the relevant clinical data.

PROGRESS IN PURSUIT OF OUR GOAL

As a normal cell is transformed into a cancer cell, its signature changes. To identify the changes in signatures linked to major steps of tumor development, NCI is building the complete molecular

catalog of cancer through the **Cancer Genome Anatomy Project** (CGAP – see ncbi.nlm.nih.gov/CGAP). Over 44,000 new genes have been discovered through CGAP's main component, the human Tumor Gene Index (TGI). To help us better understand the genetic and molecular foundations of cancer and other human diseases, NIH is creating a **Mammalian Gene Collection** (MGC) that will enable the scientific community to obtain individual full-length, human or mouse complementary DNAs (cDNAs) for more rigorous study of individual genes, their protein products, and the role they play in human disease.

NCI has established a number of programs to develop and offer novel technologies to make molecular and analytical resources available for researchers to identify, characterize, and validate signatures. Through the **Unconventional Innovations Program** (UIP), NCI is supporting peer-reviewed, novel, high-impact ideas with the potential to revolutionize cancer research and cancer care. Five UIP contracts for “Novel Technologies for Noninvasive Detection, Diagnosis, and Treatment of Cancer” have been awarded. The UIP is complemented by the **Innovative Molecular Analysis Technologies Program**, which has awarded over 80 grants focused on development and pilot applications of new technologies for the molecular analysis of cancers and their host environment. NCI also is working with the National Aeronautics and Space Administration (NASA) to develop minimally invasive molecular biosensors and is sharing ideas on the development of other high impact technologies. The agencies host the **NASA/NCI Biotechnology Forum**, a Web-based forum that brings together NCI and NASA scientists, technologists, and engineers. Finally, to identify leads for cancer therapy and develop novel strategies for marker discovery, NCI is funding **combinatorial libraries** of small molecules, peptides, and antibodies. The libraries can be screened to identify molecules (ligands) that bind differently to tumor and normal cells, or bind differently between tumors of varying malignant potential. These ligands can be used for new approaches to cancer diagnosis and prognosis.

Clinical specimens are a critical resource for the discovery and research application of molecular signatures to problems in cancers. NCI initiatives

in this area include **Cooperative Tissue Resources for Breast and Prostate Cancers** and the **Cooperative Human Tissue Network**. The Institute is increasing access through a **Tissue Expediter**, who helps researchers locate the specimens and related clinical data they need. NCI also has created the **Shared Pathology Informatics Network**, a consortium of institutions connected by a model Web-based system that both provides direct access to data related to archived specimens and protects patient confidentiality. Tissue resources will likewise be key as we conduct tissue microarray technology research and development through the **Tissue Array Research Program** (TARP – see cancer.gov/tarp), supported by NCI and the National Human Genome Research Institute (NHGRI). Tissue microarrays can hold hundreds of tissue samples on a single slide, and are an important tool in the search for and validation of molecular signatures. TARP will produce multi-tumor screening tissue microarrays for the research community starting in Fall 2000, serve as an arraying facility for groups with unique tissue materials, and disseminate tissue microarray technology by providing training. TARP efforts will be supported by NCI's **Advanced Technology Center** (ATC) where scientists use new technologies to address biological, clinical, and genetic questions pertinent

to human cancers. The ATC, which also houses CGAP, is a premier facility for developing tools for molecular expression profiling studies.

Using experimental animal models that parallel the behavior of human cancer and its response to preventive and therapeutic interventions will greatly improve our understanding of molecular changes that contribute to cancer and could enhance our ability to evaluate biomarkers prior to clinical application. To meet this need, NCI launched the **Mouse Models of Human Cancer Consortium**, which is developing and making available to the research community characterized and validated mouse models. In addition, NCI's **Mouse Cancer Genome Anatomy Project** (mCGAP) is investigating molecular determinants of cancer in the mouse for comparative studies in human tumors. The materials developed are being made publicly available to support efforts to identify mouse modifier genes involved in cancer etiology.

To identify and evaluate molecular biomarkers and technologies for earlier detection and risk assessment of all major cancers, NCI established the **Early Detection Research Network** (EDRN – see edrn.nci.nih.gov). The EDRN is a national network of academic and industry investigators with expertise in laboratory and clinical sciences, biostatistics, informatics, and public health. Research

SPOTLIGHT ON RESEARCH

A New Detection Tool – Looking for DNA Mutations

When cancer is detected early, lives are saved. But finding a tumor in its earliest stages of development, when it is composed of only a few cells, is like searching for a needle in a haystack. Scientists funded by NCI's Early Detection Research Network (see above) have developed a novel approach to early detection based on identifying genetic mutations found in the DNA housed in a cell's mitochondria – the specialized parts of a cell responsible for generating energy.

These scientists found that mitochondrial DNA mutations observed in the body fluids of cancer patients were identical to those found in their primary tumors. They first analyzed mitochondrial DNA from bladder, head and neck, and lung tumors and identified specific mutations linked to these cancers. Then, searching for similar mutations, they studied urine, saliva, and cells washed from the lungs of 20 patients with these cancers. The researchers detected mitochondrial mutations in all of the patients with bladder and lung tumors and most of those with head and neck tumors. In the past, researchers have found similar

funded through EDRN's 18 Biomarker Developmental Laboratories, three Biomarker Validation Laboratories, eight Clinical/Epidemiology Centers, and Data Management and Coordinating Center already is yielding results. EDRN-funded researchers have discovered a novel approach for detecting cancer based on mutations in mitochondrial DNA found outside a cell's nucleus. (See Spotlight on Research below.)

The traditional classification of human tumors is based on tumor structure, but structure alone does not always accurately predict a tumor's biological behavior, treatment response, or prognosis. NCI is seeking a more clinically predictive and useful classification system through the **Director's Challenge: Toward a Molecular Classification of Tumors**. Investigators funded by this initiative are creating comprehensive molecular profiles of tumors using DNA, RNA, or protein-based technologies. These profiles will identify clinically important tumor subsets and will provide more informative molecular classification schemes for human cancers. To validate new approaches to diagnosis, prognosis, and prediction of response to therapy, NCI has launched the **Program for the Assessment of Clinical Cancer Tests**. The program is a major expansion of NCI efforts in this area and removes the most frequently recognized barriers to progress

in translating new discoveries into clinical practice. It helps NCI and investigators focus on linking technological availability with clinical need.

For more information on NCI's Signatures initiatives, go to cancer.gov/initiatives.

Budget Increase Request for 2002 Defining the Signatures of Cancer Cells

1. Expand the development and availability of molecular and analytic resources	\$35.5 M
2. Establish and make tissue resources available to researchers.	17.5 M
3. Develop molecular signatures to study and validate animal models.	8.5 M
4. Develop novel technologies for early detection and determination of biomarkers.	14.0 M
5. Validate molecular classification schemes and develop new diagnostic tests.	13.3 M
6. Characterize aberrant molecular interactions in cancer.	18.0 M
Management and Support	4.0 M
Total	\$110.8 M

matching mutations in primary tumors and in body fluids when looking at DNA in a cell's nucleus. However, a cell has just one nucleus but many mitochondria, making mitochondrial mutations much easier to find and potentially more ideal avenues for detection.

Researchers envision using mitochondrial DNA for cancer screening. For example, a person at higher risk of developing lung cancer because of tobacco use might provide his or her doctor with a sputum sample. The initial sample

would be analyzed to obtain a baseline description of the individual's mitochondrial DNA. In subsequent visits, new sputum samples would be collected and compared to the baseline for changes. If changes indicating cancer were observed in the mitochondrial DNA, doctors would be in a better position to intervene while the cancer is in an early stage. The identification of mitochondrial DNA mutations in a variety of tumors represents an opportunity to develop new, noninvasive screening approaches for cancer based on analysis of easily collected body fluids.

THE PLAN – DEFINING THE SIGNATURES OF CANCER CELLS

Goal

Generate a complete catalog of the distinguishing molecular signatures of normal, precancerous, and cancer cells at all stages in all tissues, and use the catalog to develop diagnostic techniques for the earliest detection of precancerous lesions and cancers; develop signature-based therapies; and identify subsets of patients with different prognoses to predict therapeutic response.

Objectives and Milestones for Fiscal Year 2002

- 1. Expand the development and availability of molecular and analytic resources. \$35.5 M**
 - Complete the TGI for genes expressed in cells at all stages of tumor development. \$2.50 M
 - Continue development of the MGC for full-length human and mouse cDNAs. \$5.00 M
 - Double the number of Phased Innovation Awards to develop technologies relevant to discovering and measuring molecular signatures of cancer and precancer. \$5.00 M
 - Expand development of biosensors for detecting human cancer and cancer development through the UIP. \$20.00 M
 - Continue development of databases and analytic tools for comprehensive molecular analysis. \$3.00 M

- 2. Establish and make available to researchers tissue resources to maximize the practical application of molecular signatures to problems in treating cancer. \$17.5 M**
 - Establish a national tissue resource system for all major cancers, including cancers of the lung, breast, prostate, colon, head and neck, brain, soft tissue, blood, bone, the gynecologic and genitourinary systems, and childhood malignancies. \$4.00 M
 - Develop and expand tissue repositories of precancerous lesions in all major cancers. \$4.00 M
 - Use Phased Innovation Awards to develop tissue preservation and sample preparation methods to increase their utility and compatibility with new technologies for cancer and precancer. \$4.00 M
 - Support tissue microarray technology development and expand the TARP for distributing tissue microarrays. \$2.00 M
 - Develop a Web site with query and search capabilities to help investigators locate appropriate national tissue repositories. \$0.30 M
 - Enhance the Web-based system to query pathology information systems including pathology standardization and agreement on common data elements. \$2.50 M
 - Provide automatic encryption features for personal identifiers associated with tissue resources. \$0.20 M
 - Develop public education materials about tissue donation for research. \$0.50 M

- 3. Develop molecular signatures to study and validate animal models for human cancer. \$8.5 M**
 - Complete the mCGAP to define the molecular anatomy of mouse cancer models. Link the mCGAP to the mouse phenotype and tumor databases to provide a continuum of linked descriptors of cancer. \$3.00 M

<ul style="list-style-type: none"> ■ Enhance informatics tools to link the human and mCGAP data for use in validating mouse models as predictors of human cancer development and progression. \$0.50 M ■ Continue development of preclinical mouse models and fund systematic analysis and phenotyping to validate them. Use these models to validate new molecular-based approaches for early detection, diagnosis, treatment, and prognosis of human cancer. \$5.00 M 	
<p>4. Support novel technology development for early detection and for determining biomarkers of precancerous lesions and cancer.</p> <ul style="list-style-type: none"> ■ Expand discovery, development, and validation of new early detection tests for all major human cancers through the EDRN. \$8.00 M ■ Develop high throughput technologies for isolating and enriching cells shed in body fluids. \$2.00 M ■ Provide supplemental funding for biomarker evaluation to groups conducting prevention and therapy studies. \$4.00 M 	\$14.0 M
<p>5. Validate molecular classification schemes of cancer and develop new diagnostic tests.</p> <ul style="list-style-type: none"> ■ Fund expanded validation programs for each major cancer site as results emerge from the Director’s Challenge and other programs. \$10.00 M ■ Validate new diagnostic approaches through a Program for Assessment of Clinical Cancer Tests to provide the research community with a means to evaluate and validate signatures with possible diagnostic value. \$3.25 M 	\$13.3 M
<p>6. Support basic research aimed at characterizing aberrant molecular interactions in cancer.</p> <ul style="list-style-type: none"> ■ Generate a comprehensive map of all cellular signal transduction pathways and their links to one another through a Signal Transduction Annotation Consortium. \$3.00 M ■ Support basic research efforts for analysis of: higher order cellular architecture that may be perturbed in cancer; organization of chromosomes into chromatin and their localization within the nucleus; the structure and function of molecular machines; and structure and function of membranes. \$5.00 M ■ Fund 10 Phased Innovation Awards to develop technologies for analyzing cell-cell interactions and communication that might be perturbed in cancer. \$5.00 M ■ Develop an informatics system that will enable the modeling of dynamic and integrated cellular functions by establishing a “Virtual Cell” Consortium. \$5.00 M 	\$18.0 M
Management and Support	\$4.0 M
	Total \$110.8 M

4

Molecular Targets of Prevention and Treatment

THE OPPORTUNITY

Our systematic search for drugs to combat cancer began about 60 years ago. Throughout most of this search, our understanding of cancer has been limited by available technologies. The microscope, for example, enabled us to see the structure of the cancer cell, but revealed nothing about what actually makes a cell cancerous or about how the inner workings of the cancer cell differ from a normal cell. As a result, techniques for identifying drugs to prevent or treat cancer were limited to tests that measured inhibition of cancer's development or its growth in animals or test tubes. Despite these limitations, scientists have identified several synthetic and natural substances that appear to thwart cancer development, and they have developed drugs that, alone or with surgery or radiation, can cure some cancers in people and ease symptoms in others.

Yet, most of the common tumors of adults do not respond well to the treatments available today. And even when treatments successfully shrink tumors or eliminate them from the body, they can cause a variety of short- or long-term side effects that can have a devastating impact on a patient's quality of life. Many of chemotherapy's most severe toxic effects stem directly from their non-selective nature; most available compounds that inhibit tumor cell growth also inhibit the growth of healthy cells. However, drugs that target the molecular differences between tumor and normal cells – the altered genes or proteins or corrupted pathways – promise to be less toxic and more effective than our current drugs.

The situation for prevention is similar. Knowledge of the precise molecular steps that characterize premalignant change will provide the foundation for our search to find agents that reverse these changes or block the steps critical to the full

development of cancer.

Scientists working to discover effective prevention and treatment agents have always faced a formidable barrier: not knowing precisely what cancer is. Now, with the evolution of molecular biology and the emergence of new technologies, we are gathering remarkable knowledge about the nature of a cancer cell and the molecular changes that occur before and during a tumor's development. The extraordinary opportunity before us to discover and exploit molecular targets for cancer prevention and treatment arises from the convergence of scientific advances in the areas of cancer biology, synthetic and biosynthetic chemistry, high throughput screening, and medical imaging.

G O A L

Accelerate discovery, development, and testing of prevention and treatment agents that target the molecular changes of cancer.

Cancer Biology

Evolving knowledge of how molecules and pathways in premalignant or fully malignant cells differ from their normal counterparts is enabling us to refine human tumor classification in terms of molecular changes and also is giving us a new strategy for cancer drug discovery. Every point of difference between premalignant or malignant cells and their normal counterparts is a potential target of opportunity for drug discovery – a molecular target of prevention or treatment. Targets also may be revealed by understanding the consequences of fundamental molecular changes in cancer, such as those that spur blood vessel growth to nourish tumors. Still others are normal molecular machines that take on particular significance in the context of cancer, such as hormone or growth factor systems.

Synthetic Chemistry

Traditionally, the chemicals used in anti-cancer drugs have come from nature – from tropical rain forests or organisms in the sea or the soil. Using recently developed techniques, chemists now are able to create enormously diverse collections of

compounds, and we can screen both natural and synthetically derived chemicals for possible anti-cancer effects.

Biosynthetic Chemistry

Synthetic chemists have long been able to manipulate small molecules to produce useful medicines. Now, the biotechnology revolution has cleared the way for biochemists to mix and match genes to design synthetic proteins. Changing proteins in cells is a crucial step, since proteins form the “messages” that make up communication pathways that determine a cell’s healthy or aberrant behavior. Now scientists can change the messages sent by protein molecules, creating a new class of drugs to be tested for anti-cancer activity.

High Throughput Screening

Biotechnology advances also have made it possible to devise highly sensitive, efficient tests for virtually any biological process. These tests, or “smart” assays, can be used many different ways. For example, they can be used to screen cell lines and tissues for the presence of particular genes, proteins, or entire pathways, an essential step in identifying the chain of events involved in every stage of cancer development. They also can be used to screen potential drugs for anti-cancer effects. Smart assays, which can screen thousands of compounds each week, can be performed on a micro scale with tiny quantities of material, using computer-driven robots to maximize efficiency.

Medical Imaging

Until now, imaging has been used in cancer research and care to gain information about the occurrence, size, and location of tumors. Refinements in imaging technology are now allowing us to watch molecular processes within the cell unfold, with unprecedented vividness and accuracy. Imaging techniques are being developed to tell us not only the location of a tumor but the kind of molecules it contains and how its biochemical pathways work. (See [p. 69](#) for the Imaging Extraordinary Opportunity.)

The convergence of advances in these fields presents us with the opportunity to revolutionize cancer drug discovery and develop a whole new generation of cancer preventives and treatments –

drugs that target the molecular features of cancer. To ensure our success, however, we need to create unprecedented conceptual and functional links among drug discovery, development, and clinical testing. To understand why, one must consider the main questions that researchers need to pursue about a new drug’s effect on malignant or precancerous cells: Does the drug kill the cancer or effectively block its growth and spread? What part of the cell’s complex machinery does it disrupt, and how is this disruption related to its anti-cancer effect? Tools to address this second question have been crude and inadequate, so our clinical testing has focused only on the first.

We must gather the knowledge and develop the tools to answer both of these questions. When we can, we will be able to better address some of the most important questions in cancer therapeutics: If a drug is working well, why is it working, and if not, why not? Are we giving a person the right amount, or too much, or too little? Do we have to give people the maximum amount of a drug that they can tolerate, or can we judge the right amount by whether the drug is getting to the tumor and affecting its target? Will the drug harm the patient now or in the future? Only when we can answer these questions will we be able to predict who is likely to respond to a particular treatment and who will not. Moreover, information from the clinic and from the laboratory will reinforce each other, providing the basis for designing even better drugs in the future.

Budget Increase Request for 2002 Molecular Targets of Prevention and Treatment

1. Identify, characterize, validate, and produce targets for drug discovery.	\$16.5 M
2. Synthesize or acquire molecules for use in drug screening efforts.	30.5 M
3. Facilitate the steps to turn a promising compound into a drug.	28.0 M
4. Facilitate partnering.	41.5 M
5. Support special interdisciplinary initiatives.	25.0 M
Management and Support	5.0 M
Total	\$146.5 M

PROGRESS IN PURSUIT OF OUR GOAL

Identifying molecular targets research as an extraordinary investment opportunity reflects NCI's commitment to exploit the molecular underpinnings of cancer to achieve more effective prevention and treatment interventions. We have launched a number of new initiatives and continue to support ongoing programs to stimulate research in this critical area.

To encourage creative investigations for *identifying, characterizing, and validating promising new molecular targets*, NCI has established **Molecular Target Drug Discovery (MTDD) grants** in various scientific disciplines to identify novel molecular targets for prevention and treatment, validate the targets as a basis for cancer drug discovery, and develop tests to detect the effects of these agents on their targets.

Newly developed chemical and biological combinatorial techniques are enabling scientists to create, over the course of weeks or months rather than years, millions of chemically diverse structures with potential anti-cancer effects. And biotechnology advances are enabling researchers to mix and match genes to design synthetic proteins, creating a new class of potential anti-cancer agents. To fully exploit the *new opportunity to synthesize or acquire large numbers of possible drug molecules*, NCI is con-

tinuing its support of six **Biology-Chemistry Centers**, two of which were funded in Fiscal Year 2000. This novel interdisciplinary program facilitates collaborations among top researchers in chemistry, biology, genetics, and computer science for developing and refining robotic drug production and screening technology. The Biology-Chemistry Centers already have screened hundreds of thousands of compounds.

Another ambitious effort to *develop new anti-cancer agents* is the **Rapid Access to Intervention Development (RAID)** program, designed to efficiently move novel treatment interventions developed in academic settings into the clinic. Because academic institutions commonly lack the capacity to develop drugs, promising ideas and candidate molecules cannot always move forward in the drug discovery process. The RAID program makes NCI's drug development resources available to investigators with molecules that hold promise for cancer treatment. By providing the resources needed for preclinical development of drugs and biological agents, this program removes the most common barriers between laboratory discovery and clinical testing. Products developed through RAID are returned directly to the originating laboratory for clinical trial testing. Fourteen projects were funded in Fiscal Years 1999 and 2000, and funding for additional projects is planned for Fiscal Year 2001.

SPOTLIGHT ON RESEARCH

Diffuse Large B-Cell Lymphoma: A Disease Within A Disease

Each year, 25,000 people in this country are diagnosed with diffuse large B-cell lymphoma (DLBCL), the most common form of non-Hodgkin's lymphoma (NHL). DLBCL is a form of cancer in which B cells in the immune system proliferate uncontrollably. Physicians have long questioned why standard chemotherapy cures only 40 percent of their DLBCL patients while the majority relapse and die. A team of scientists recently used the powerful new DNA microarray technology to make an intriguing discovery that is a critical key for solving this puzzle.

The scientists created a novel microarray tool, which they called the "lymphochip," by mining the Cancer Genome Anatomy Project (CGAP) database for information on over 18,000 genes important to both lymphoid malignancies and the immune system and placing them on a device similar to a computer chip. The lymphochip enabled them to compare gene activity of normal and cancerous B cells and generate gene expression profiles, or signatures, of the different cell types. After examining several different forms of non-Hodgkin's lymphoma, the scientists discovered that DLBCL cells showed two distinct patterns of gene expression, suggesting that this diagnosis actually

While RAID focuses on developing promising candidate molecules to treat cancer, the **Rapid Access to Preventive Intervention Development (RAPID)** program is providing funding and resources to scientists working to develop agents to prevent, reverse, or delay cancer development. Like RAID, RAPID is designed to quickly move novel preventive molecules and concepts from the laboratory to the clinic for efficacy testing in clinical trials. RAPID will accelerate the development process for preventive agents by providing academic investigators with the contract resources needed for pre-clinical and early clinical drug development, ensuring the efficient translation of promising discoveries even when investigators and their institutions lack the requisite development capacity or clinical expertise. Seven projects were funded through this program in Fiscal Year 2000, and we expect to fund additional projects in Fiscal Year 2001.

The many steps involved in *turning a potential anti-cancer agent into a drug appropriate for human use* can take years and an investment of several million dollars. The process includes discovery, efficacy testing, development of lead agents, pharmacology and toxicology studies of the potential drug, Investigational New Drug (IND) application filing with the Food and Drug Administration, and clinical evaluation. To support small business participation in this process, NCI established the **Flexible**

System to Advance Innovative Research (FLAIR) to provide small businesses the budgets and time required to identify promising agents and develop them into drugs that can be evaluated clinically.

To *discover, develop, and validate innovative tools* to help scientists determine whether a potential agent actually affects an intended molecular target, NCI has set aside funding for **Interdisciplinary Research Teams for Molecular Target Assessment (IRTMTA)**. Each multidisciplinary team will focus on a critical biological process thought to contain high priority targets for cancer prevention or treatment drug discovery. They will work to develop tools, probes, assays, and imaging approaches to assess the effects of drugs on their targets.

NCI recently announced the **Molecular Targets Laboratory (MTL) initiative** that will focus intensively on developing a resource of biological assays and chemical probes for biological studies of cancer. The MTLs will emphasize collaboration between chemists and biologists to produce libraries of potential anti-cancer compounds for public distribution, develop screening assays suitable for high throughput screening of chemical libraries of potential agents, and confirm a drug's ability to alter the drug target in cancer cells.

For more information on NCI's Molecular Targets initiatives, go to cancer.gov/initiatives.

has lumped together two subtypes of NHL. While unable to distinguish one from the other under a microscope, the tool conventionally used for diagnosis and cell typing, scientists now are able to use advanced technology to sort out these two biologically distinct subtypes of lymphoma and to subsequently identify two distinct clinical courses that DLBCL can take. Although more research is needed, scientists are optimistic that expression signatures will lead them to more precise diagnoses and ultimately to more effective treatments for specific subtypes of this disease.

Over the coming years, we expect to be able to use gene expression signatures like these to vastly improve our ability to diagnose, classify, and treat not only lymphoma but all types of cancer. By analyzing differences at the molecular level, we can identify the genes and cell pathways that are important to cancer development and progression. These molecular differences will provide the clues to early detection and diagnosis and serve as the targets of present and future cancer drugs.

THE PLAN – MOLECULAR TARGETS OF PREVENTION AND TREATMENT

Goal

Accelerate the discovery, development, and testing of prevention and treatment agents that target the molecular changes underlying the various stages of cancer initiation and progression.

Objectives and Milestones for Fiscal Year 2002

- 1. Identify, characterize, validate, and produce targets in precancerous and cancerous cells for drug discovery.** **\$16.50 M**

We will identify novel targets that represent critically vulnerable sites – the true Achilles’ heels – within cells, determine the role they play, validate their biological importance in cancer growth, and mass produce promising targets for use in testing the potential effects of various agents.

 - Expand the MTDD program to include 10 grants in each of 3 focus areas involved in cell signaling events: cell cycle regulation, cell death and immortality, and cell invasion and metastasis. \$9.00 M
 - In conjunction with the Mouse Models of Human Cancer Consortium, develop transgenic animal models (mice genetically altered to express human genes relevant to cancer) to verify the potential drug responsive characteristics of selected targets and define their associated pathways. \$3.00 M
 - Co-fund with the National Institute for General Medical Sciences the expansion of technology in the National Beam Laboratories to enable researchers to rapidly determine the structure of important molecular targets, thereby permitting computer modeling of potential agents. \$4.50 M

- 2. Synthesize or acquire large numbers of diverse candidate molecules for use in drug screening efforts.** **\$30.50 M**

We will encourage chemists and biologists to work collaboratively to synthesize novel structures aimed at defined molecular targets, support expanded efforts to collect candidate agents from nature, and promote research efforts to synthesize biological agents (e.g., vaccines, recombinant proteins) directed at target molecules.

 - Procure and distribute libraries of chemically diverse compounds to cancer drug discovery researchers, including MTDD grantees, to rapidly determine the effectiveness of these compounds against novel targets in drug screens guided by target structure. \$5.00 M
 - Expand the collection of natural product extracts from threatened ecologic niches and previously unexplored biorealms. Increase operations to augment the library of available natural product extracts to assure a constantly renewable supply of this valuable resource. Create a centralized distribution center for formatted natural product extracts. \$8.00 M
 - Expand support for RAID and RAPID to assist investigators in producing sufficient quantities of potential biological agents for testing. Partner investigators with appropriate commercial, government, or academic production facilities. \$6.00 M
 - Create a repository of public domain libraries of biological agents (e.g., peptides, carbohydrates) relevant to target cells or organs. \$4.00 M
 - Create 2 or 3 Centers of Excellence in Biologics to support approaches for designing, producing, validating, and clinically testing vaccines, viral vector constructs for agent delivery, and/or recombinant proteins directed at cancer-related target molecules. \$7.50 M

<p>3. Facilitate the steps necessary to turn a promising target-directed compound into a drug appropriate for human use.</p> <ul style="list-style-type: none"> ■ Fund studies of promising target-directed compounds to determine toxicity and modify them as needed to be more effective and well tolerated by patients. Information gleaned from target structure and animal model studies will assist in this process. \$8.00 M ■ Assist small businesses in cancer drug discovery by expanding the FLAIR program to develop novel approaches to molecular toxicology, formulation advances, and clinical evaluation and by using a RAID-like process to provide contract research resources to advance concepts. \$6.00 M ■ Expand the IRTMTA from 2 or 3 to at least 10 centers to develop a “toolbox” of valid assays for assessing a drug’s affect on its intended target, thereby speeding movement of candidate drug molecules to the clinic. Develop a formal process for clinical investigators to access expertise for developing assays in support of early clinical trials focused on assessing whether drugs affect their molecular target of reference. \$14.00 M 	<p>\$28.0 M</p>
<p>4. Facilitate partnering of academic, commercial, and government resources to promote cancer drug discovery and development.</p> <ul style="list-style-type: none"> ■ Expand from 12 to 16 the number of National Cooperative Drug Discovery Groups to facilitate partnerships with industry and academia to foster multidisciplinary approaches to the discovery of novel prevention or treatment strategies. \$16.00 M ■ Support the creation of publicly available databases and data mining tools for compound and target information. These databases and tools will provide an informatics infrastructure for MTDD and MTLs and serve as an archive for MTDD and MTL information. Sponsor yearly interdisciplinary chemistry/biology/genomics/proteomics workshops for academic and small business researchers to enhance interactions. Design and build a Web-based workshop to continue such interactions. \$3.50 M ■ Double the number of academic Phase I trials supported by NCI and promote partnering between NCI-funded centers and commercial firms with suitable test agents. Provide infrastructure to centers doing Phase I studies to allow verification of the molecularly targeted nature of drug action. \$7.00 M ■ Establish 5 new high priority Phase II trials through Specialized Programs of Research Excellence (SPOREs) and cancer centers focusing on breast, prostate, colorectal, other gastrointestinal, and gynecologic cancers, and leukemia/lymphoma. \$15.00 M 	<p>\$41.5 M</p>
<p>5. Support for special interdisciplinary initiatives</p> <ul style="list-style-type: none"> ■ Increase resources allocated to the MTLs to develop a resource of biological assays and chemical probes for biological studies of cancer. 	<p>\$25.0 M</p>
<p>Management and Support</p>	<p>\$5.0 M</p>
Total	\$146.5 M

5

Research on Tobacco and Tobacco-Related Cancers

THE OPPORTUNITY

The numbers are alarming. An estimated 450,000 people in the U.S. will die this year alone from tobacco-related diseases – the most preventable and costly cause of death in our Nation. Every day more than 3,000 youths start smoking, placing themselves at increased risk for a host of cancers, particularly lung cancer, which causes approximately 160,000 deaths a year. Mouth, pharynx, larynx, esophagus, pancreas, cervix, kidney, and bladder cancer, as well as heart disease and many other conditions are all associated with tobacco use. Of those who continue to smoke, approximately half will die prematurely, losing an average of 20 to 25 years of their life expectancy. The global picture is even more sobering: More than one billion people smoke worldwide and an estimated three million die annually from tobacco-related illness. By 2025, the number of deaths is expected to reach ten million per year.

These statistics illustrate dramatically that the use of cigarettes, cigars, pipes, and smokeless tobacco products is a major worldwide threat to health that must be addressed. Although their risk for lung cancer remains higher than if they never had smoked, strong evidence shows that people who stop smoking – regardless of age – live longer than those who continue to smoke.

Developing Optimal Prevention and Cessation Strategies

Studies indicate that while the majority of smokers want to stop smoking completely, they struggle to quit. Most adults who smoke regret ever starting. It is critical that strategies be developed to prevent people from ever starting to smoke and help those who currently smoke to stop.

The past three decades have brought many achievements in this area – we have developed and implemented physician training and office protocols for smoking cessation, confirmed the effectiveness of primary care medical and pharmacologic interventions, and developed both effective self-help interventions and tailored interventions designed to meet the needs of individual smokers. Mass media interventions to reach large numbers of people with prevention and cessation messages have been developed, and strategies to reach minority, ethnic, and high-risk populations have been tested. Recent large-scale programs, like the Community Intervention Trial for Smoking Cessation (COMMIT) and the American Stop Smoking Intervention Study (ASSIST) have shown both the potential and the limitations of community and state tobacco control interventions for changing attitudes about tobacco use, changing tobacco use behaviors, and reducing the tobacco-related cancer burden. Still, we do not fully understand the most critical elements of tobacco prevention and treatment strategies, their timing, how best to target high-risk subgroups and settings, and how to tailor messages and materials appropriately for different populations.

G O A L

Understand the causes of tobacco use, addiction, and related cancers and apply this knowledge to their prevention and treatment.

Identifying and Targeting Populations at High Risk for Tobacco-Related Cancers and Nicotine Addiction

We have made enormous progress in understanding at the molecular level the transformation of a normal cell to a cancer cell following exposure to tobacco carcinogens. Scientists have identified many cancer-causing agents contained in tobacco smoke and shown that different tobacco products and methods of nicotine delivery influence the type and quantity of exposure to these agents.

Researchers also have determined that these multiple agents seem to induce similar changes,

regardless of the cell's location in the body. The challenge now is to learn more about how and why elements in tobacco smoke target particular genes and how tobacco-induced cellular damage initiates and promotes cancer development. Such knowledge will help us identify precancerous lesions and markers that may predict tobacco-induced cancer. Identifying markers that detect DNA damage and other antecedents of cancer will enable us to test different prevention and treatment strategies and develop new early detection methods.

This research also could provide important insights into why some people may be particularly vulnerable to harm from tobacco. For example, women develop more lung cancers than men per cigarette smoked, and certain ethnic groups also appear to be at increased risk for lung cancer. While the reasons for these differences are not clear, smokers with certain gene variants are more likely to develop lung cancer. New preclinical models are needed to enable us to identify these harmful variants that lead to increased susceptibility to tobacco-related cancers. Using this information and knowledge of how inherited susceptibilities and tobacco exposure in combination contribute to cancer, we will be able to develop specific prevention and detection strategies for vulnerable individuals.

Growing evidence indicates that genes interact with environmental factors to influence whether an individual will start smoking, how early he or she will start, and how difficult it will be to quit. Just as we now know more about the biological basis of tobacco-related cancers, we also have learned a great deal about the psychosocial, biobehavioral, and biological determinants of tobacco use and addiction. We know, for example, that adolescent tobacco use is tied to peer and family influences and low self-esteem. We know that continued smoking by adults is associated with nicotine addiction, depression, and stress. Recent research breakthroughs have provided important insights into the biological basis of tobacco use and nicotine addiction, including the role of genetic factors in nicotine metabolism. For example, certain genes modify nicotine metabolism and regulate brain chemicals that affect the pleasurable feelings triggered by nicotine. By determining how these preexisting vulnerabilities interact with sociocultural and psychological influences on tobacco use, and by improving our ability to assess risks quantitatively, we will be

able to develop more effective prevention and cessation interventions and tailor these interventions to the people most likely to benefit from them. We also will be able to identify effective new drugs and combinations of proven drugs for treating nicotine addiction. Combining pharmacologic and behavioral tailoring may prove particularly effective in accelerating smoking cessation rates.

Capitalizing on Social, Legal, and Public Policy Developments

Important social, legal, and public policy developments are converging with scientific advances to create a unique opportunity to tackle tobacco use. Public attitudes reflect decreasing acceptance of tobacco use as a social norm. Government agencies, academic institutions, and professional and voluntary organizations are making major commitments to reduce tobacco use and exposure to tobacco carcinogens. Through lawsuits, states are recovering billions of dollars lost to the treatment of diseases caused by smoking. However, while state political leaders have been urged to use these funds to expand tobacco control programs, they almost certainly will use most of the funds to address other priorities. This dilemma underscores the need for NCI to expand its investment in tobacco control research to ensure that the best scientific evidence informs state and community programs.

In summary, we have an unprecedented opportunity to reduce the enormous burden of tobacco use on our Nation's public health. The investment proposed here will enable us to gather knowledge that

Budget Increase Request for 2002 Research on Tobacco and Tobacco-Related Cancers

1. Define the biological, behavioral, and social bases of tobacco use and addiction.	\$12.0 M
2. Understand the interplay among tobacco, other exposures, and host susceptibility on cancer risk.	23.0 M
3. Develop, test, and disseminate more effective interventions to prevent and treat tobacco use and tobacco-related cancers.	29.0 M
Management and Support	3.0 M
Total	\$67.0 M

Extraordinary Opportunities

THE PLAN – RESEARCH ON TOBACCO AND TOBACCO-RELATED CANCERS

Goal

Understand the causes of tobacco use, addiction, and tobacco-related cancers and apply this knowledge to their prevention and treatment.

Objectives and Milestones for Fiscal Year 2002

1. **Expand efforts to define the biological, behavioral, and social bases of tobacco use and addiction.** **\$12.0 M**
 - Develop and implement specialized surveys and incorporate biospecimen collection in cohort studies to better understand youth tobacco use and addiction. \$4.00 M
 - Establish regional repository resources to house large numbers of biospecimens and encourage collaborative studies to identify genetic predisposition for tobacco use and addiction. \$4.00 M
 - Conduct national tobacco control surveys on activities that impact tobacco control through supplements to the Current Population Survey. The data, covering diverse populations, are used increasingly by Federal and non-Federal researchers to assess progress in cancer control. \$2.00 M
 - Create a public use research resource of regional, state, and local tobacco-related policy and legislation to expand capacity to assess the effect of these factors on regional and local tobacco control progress. \$2.00 M

2. **Accelerate progress in understanding the interplay among tobacco, other exposures such as alcohol and asbestos, and host susceptibility on cancer risk.** **\$23.0 M**
 - Expand existing prospective studies by incorporating biospecimens, developing standard measures and shared data instruments, and supporting cooperative efforts in order to identify and characterize genetic and biological factors affecting vulnerability to tobacco-related cancers. \$10.00 M
 - Fund innovative studies to determine how tobacco use contributes to cancers other than lung and oral cancers, such as pancreatic, cervical, kidney, and bladder cancers. \$5.00 M

will inform policy makers and public health practitioners about the best strategies for preventing and treating tobacco use and tobacco-related cancers.

PROGRESS IN PURSUIT OF OUR GOAL

NCI has a number of projects underway in its intramural cancer epidemiology and genetics program to better understand the causes and mechanisms of tobacco-related cancer. NCI is conducting large case-control studies of lung, bladder, renal,

non-Hodgkin's lymphoma, biliary tract, and gastric cancer. These studies include genetic and biomarker components to complement traditional epidemiological approaches for assessing risk. Population-based cohort studies on lymphomas, leukemias and cervical cancer are assessing the role of tobacco use. The Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer study is evaluating screening strategies for multiple smoking-related cancers and for colonic polyps, a pre-cancerous condition related to tobacco. A study of family members with Von Hippel-Lindau syndrome, an inherited cancer syndrome, is establishing whether tobacco influences

- Support the development of animal models for tobacco-related carcinogenesis. \$1.00 M
- Support research that combines population and family approaches to better understand the interplay of genes and environment in tobacco-related cancers. \$5.00 M
- Collaborate with other NIH Institutes to support studies to further define the adverse health effects of environmental tobacco smoke exposure. \$2.00 M

3. Develop, test, and disseminate more effective interventions to prevent and treat tobacco use and tobacco-related cancers, especially in high-risk individuals and groups. \$29.0 M

- Support pilot projects that incorporate biomarkers in developing and evaluating chemopreventive agents in populations of former smokers at high risk for tobacco-related cancers. \$3.00 M
- Support the development of biomarkers of tobacco exposure and risk. Such correlative laboratory projects will complement activities ongoing in the Early Detection Research Network. \$3.00 M
- Fund studies to develop and test new behavioral, pharmacological, and combination therapies to treat nicotine dependence, with special emphasis on populations at high risk. \$6.00 M
- Support rapid, standardized evaluations of current tobacco cessation programs for adolescents and young adults. \$2.00 M
- Support studies in collaboration with public and private tobacco research funding organizations to identify successful tobacco use prevention interventions. \$5.00 M
- Expand support for research to evaluate the impact of new state and community tobacco control programs. \$10.00 M

Management and Support

\$3.0 M

Total

\$67.0 M

cancer in cancer-prone families. To advance our understanding of genetic and environmental interactions that influence smoking behavior and lung cancer in particular, NCI will support a **genetic epidemiology of lung cancer and smoking study**. This interdisciplinary case-control study will explore how tobacco and genes influence both lung cancer and smoking by incorporating the study of siblings and an extensive biospecimen collection.

Seven **Transdisciplinary Tobacco Use Research Centers** (TTURCs) – launched in 1999 under the joint sponsorship of NCI, the National Institute on Drug Abuse, and the Robert Wood Johnson Foundation – are helping to provide the needed

infrastructure for tobacco research across many disciplines. TTURC researchers are tackling a wide range of topics, including genetic susceptibility, animal models of behavior, sociocultural factors, innovative treatments, and research on health care policy and bioethical implications of tobacco control. The Centers will accelerate tobacco control intervention development, speed the transfer of these approaches to communities nationwide, and train a new generation of tobacco control researchers.

To further understand youth tobacco use and addiction, NCI, in collaboration with other NIH Institutes, is supporting **youth prevention and cessation research**. This research includes projects on

adolescent tobacco use prevention, experimentation related to the onset of regular tobacco use, dependence and withdrawal, and cessation and treatment of tobacco use.

Tobacco-related deaths among U.S. women continue to rise. NCI is supporting several **studies on tobacco use and addiction in women**. Studies on reducing tobacco use by pregnant women are focused on helping low-income women quit, testing the ability of women's partners to assist them in quitting, and preventing relapse after delivery. Another study examines the relationship between smoking and major depressive disorder, a problem that disproportionately affects women. NCI also is funding a major study of African American women's health that includes an examination of smoking behavior.

We still need to know how best to design and conduct state and community tobacco control programs. NCI is supporting 12 new research projects on **innovative tobacco prevention and control interventions at the community, state, or multi-state level**. Questions being addressed concern the impact of media campaigns on tobacco use behaviors, readiness to quit, and attitudes and how to tailor media and policy interventions to influence high-risk groups.

NCI is working with public and private partners to build a comprehensive and integrated surveillance system to monitor tobacco control progress at the local, regional, and national levels. Through the **Tobacco Use Supplement to the Current Population Surveys (CPS)**, final data from the 1990s will be made available by the Census Bureau in Fall 2000 as a public use data resource (www-dccps.ims.nci.nih.gov/ARP/RiskFactor/tobacco.html). NCI will provide supplements to existing tobacco control grants to encourage researchers to analyze these data. NCI also is beginning pilot work to determine the best approach to creating a public use research resource of regional, state, and local tobacco-related policy and legislation to expand capacity to assess the effect of various factors on regional and local tobacco control progress.

Because effective communication and information dissemination about emerging public health issues in smoking and tobacco control are critical to reducing adult and youth tobacco use, NCI established the **Smoking and Tobacco Control Monograph** series in 1991. Recent data from the Tobacco Use Supplement to the CPS have been

used extensively in this series, for example, in *Changing Adolescent Smoking Behavior* and *Cigars: Health Effects and Trends, State and Local Legislative Action to Reduce Tobacco Use*. Data from the cigar monograph were used to support the June 2000 Federal Trade Commission's requirement that the seven U.S. cigar companies include warnings about significant adverse health risks of cigar use in their advertising and packaging. These monographs can be viewed on NCI's Web site at rex.nci.nih.gov/NCI_MONOGRAPHS/LIST.HTM.

In August 2000, NCI cosponsored and participated in the **11th World Conference on Tobacco OR Health**, a meeting that brought together researchers, clinicians, public policy officials, tobacco control advocates, public health workers, and educators from around the world. The international conference showcased the state of the art in tobacco control and provided a forum for sharing ideas and developing consensus on global approaches.

About Tobacco

- Tobacco is responsible for more than 30 percent of all cancers and nearly one in five deaths in the U.S. every year.
- In the last decade, more than four million people in this country lost their lives to tobacco-related diseases, including, according to Environmental Protection Agency estimates, more than 30,000 nonsmokers who died of lung cancer caused by breathing smoke from others' cigarettes.
- Lung cancer deaths are still increasing among women.
- Over the course of their lives, current and former smokers generate an estimated \$501 billion in excess health care costs. Tobacco costs Medicare a staggering \$10 billion each year and Medicaid more than \$12.9 billion annually.
- The latest figures confirm a disturbing increase in youth smoking over the past decade. More than one-third (34.8%) of high school students reported recently using some form of tobacco.
- Adult smoking rates did not decrease from 1995-1997, but smoking increased among those 18 to 24 years of age.

Cancer Communications

THE OPPORTUNITY

We are in the midst of a communications revolution unparalleled since Gutenberg introduced movable type to the western world in the 15th century. At no other time in history has it been so easy for so many people to access such a vast wealth of information. Radio and television continue to be powerful communication tools, and the Internet has multiplied exponentially our ability to make large amounts of information available to a wide audience quickly and easily.

From primary prevention to survivorship and end of life issues, communication empowers people to make informed cancer-related decisions and to engage in behaviors that will improve their health. The Science Panel on Interactive Communication and Health convened by the Department of Health and Human Services concluded that few other health-related interventions have the potential of interactive health communications to simultaneously improve health outcomes, decrease health care costs, and enhance consumer satisfaction. Scientists and communications experts studying the process of effective communication and its impact on health for more than 25 years have produced increasingly refined theories of health communications, including those that focus on how people process health information and how they respond to cancer-related risks. These theories have been applied to interventions that have contributed to declining smoking rates among many groups in the United States, to the increasing proportions of Americans who are eating more fruits and vegetables each day, and to the larger numbers of people who are getting screened for breast, cervical, and colorectal cancers.

Despite our progress in refining health commu-

nications theories, however, major gaps remain in our understanding of how consumers use health information. We must learn how to help people distinguish important from insignificant health risks and deal with contradictory or inaccurate health messages so they can make informed choices. We must provide accurate and balanced information about all areas of cancer treatment and care, including complementary and alternative therapies.

In addition, we need to narrow the enormous gap between what is known about cancer communications and what is practiced. We must find the best ways to inform physicians, nurses, and other health care providers of emerging best practices in patient care. We must help them to become more effective communicators and to integrate cancer communications into all aspects of cancer care. The power of health communications must be harnessed to reduce cancer-related health disparities. To achieve these aims, more research is needed, and the cadre of health communications scientists and practitioners who can conduct communications research and apply the results must be expanded.

NCI, its grantees, and contractors have long been leaders in health communications. Now it is time to seize the opportunity presented by new knowledge of health behavior, new technologies, and our arsenal of proven strategies to further empower people to increase their knowledge, use the health care system more effectively, and understand and modify their health risk behaviors. By increasing patient access to and participation in clinical trials, we also can speed the pace of discovery. Through these efforts, we will have a far richer understanding of how people use communications technologies of all kinds, and we will use that understanding to improve outcomes in cancer prevention, early detection, treatment, and survivorship.

G O A L

Understand and apply the most effective communications approaches to maximize access to and use of cancer information by all who need it.

THE PLAN – CANCER COMMUNICATIONS

Goal

Increase knowledge about, tools for, access to, and use of cancer communications by the public, consumers, patients, survivors, and health professionals – with a special focus on diverse populations – to accelerate reductions in the U.S. cancer burden.

Objectives and Milestones for Fiscal Year 2002

1. **Support cancer communications planning, research, evaluation, dissemination, and marketing by establishing new data collection and analysis strategies.** **\$3.5 M**
 - Sponsor the Health Information National Trends Survey. \$1.00 M
 - Access relevant commercial data on use of the new media for health communications to inform NCI's planning and evaluation efforts about which audiences use which new media, and how they use them. \$1.00 M
 - Fund Pilot Projects to Overcome the Digital Divide to test strategies to increase access to and use of online and other interactive cancer communications. These competitive grant supplements will be made to existing Cancer Information Service (CIS) contractors to conduct pilot research in their regions. \$1.50 M

2. **Accelerate research, development, and interventions in cancer communications.** **\$12.0 M**
 - Support Centers of Excellence in Cancer Communications Research.
 - Provide support for investigators to diffuse and disseminate NCI-funded evidence-based interventions.

3. **Develop a menu of communication choices to meet the needs of all users, and especially to increase knowledge about, tools for, access to, and use of these choices by diverse populations.** **\$6.0 M**
 - Conduct a series of pilot tests to explore the feasibility of new directions, using different CIS offices and cancer centers as test beds. \$3.00 M

PROGRESS IN PURSUIT OF OUR GOAL

NCI is already making progress in pursuit of our cancer communications goal. For example, we are taking the lead on developing the **Health Information National Trends Survey (HINTS)**, the first nationally representative survey of the American public – with emphasis on underserved populations – about their access to and use of cancer-related health information. NCI is assisted in

this biennial, longitudinal data collection effort by national experts in health communications and representatives of other parts of the Department of Health and Human Services, including the Centers for Disease Control and Prevention, the National Institute for Occupational Safety and Health, and the National Library of Medicine at NIH.

NCI is conducting ten research projects focused on maximizing effective cancer communications through **message tailoring** and increasing the impact of **behavioral counseling** on cancer control

- Develop new communication products to facilitate cancer communications for the public, patients and their caregivers, underserved populations, advocacy groups, health professionals, and cancer communicators. Continue work with the AHRQ to fund research on decision aids, and link with Pilot Projects to Overcome the Digital Divide to promote dissemination and use of interactive communication tools and collect information on current levels of and barriers to use. \$3.00 M

4. Increase the Nation’s capability and capacity for cancer communications by training the health communications scientists, researchers, and practitioners needed to achieve our scientific and health communications objectives. \$3.0 M

- Encourage the development of interdisciplinary training programs that, at a minimum, include people in the fields of health behavior, marketing, engineering, communications, public health, and medicine. \$1.00 M
- Fund existing health communications research laboratories to conduct intensive training programs and provide opportunities for research professionals in growing areas, including risk communications and interactive health communications. These will include intensive short-term training programs, grants for interdisciplinary training, and distance learning programs. \$2.00 M

5. Enhance and refocus NCI’s communications activities to provide a comprehensive, technology-supported capability for imparting information about cancer that is easily accessible, timely, and appropriate. \$2.0 M

- Enhance the accessibility and user-friendliness of NCI’s databases and Web sites.
- Centralize the coordination of external and internal communications activities to maximize proactive responses to communications priorities and challenges, ensure optimal public access to NCI’s information resources and products, and promote NCI’s identity as an accurate source of information and as the national leader in cancer research and discovery.

Management and Support \$1.0 M

Total \$27.5 M

interventions. In collaboration with the Agency for Healthcare Research and Quality (AHRQ), we are funding a review of the research evidence on **cancer-related “decision aids”** – interventions designed to help people make specific and deliberate choices by providing information on options and outcomes specific to a person’s health status. The review will provide guidance about what research is needed in this important area.

NCI and AHRQ are co-funding a demonstration project to enhance consumer and patient use of **information about health care quality**. The inves-

tigators are developing new tools for communicating about cancer-related risks. The demonstration project will develop and test methods for providing information on quality for consumers and patients to use when making health care decisions. The projects also will evaluate the impact of strategies to provide information about quality to these audiences.

We are creating **Centers of Excellence in Cancer Communications Research** to speed advances in cancer communications knowledge. Interdisciplinary teams of researchers will develop,

implement, and evaluate strategies to improve both access to cancer information and its efficacy, effectiveness, and dissemination. The Centers will collaborate with other NCI-funded centers, such as the Comprehensive Cancer Centers, Transdisciplinary Tobacco Use Research Centers, the Special Populations Networks for Cancer Awareness Research and Training, and the Cancer Information Service (CIS).

NCI is using new technologies to implement an **integrated cancer knowledge management system**. A new **Publications Locator** lets users view and order NCI publications online from the NCI Web site. Users can access publications on various types of cancer, treatment options, clinical trials, genetics, risk factors, cancer causes, prevention, and managing side effects and pain. In addition, pilot projects are underway to develop an **online Cancer Information Service (eCIS)** that would provide another alternative for people to get answers to their questions about cancer and research findings.

Unequal access to cancer information is a critical problem for cancer communications. In 2000, NCI will provide supplemental funding, in conjunction with our CIS regional offices, for **Pilot Projects to Overcome the Digital Divide**. These projects will provide the foundation for larger scale projects to respond to the access needs of underserved populations.

NCI's Operation J-O-L-T (**Joining Organizations with Leading Technologies**) is working with numerous other groups to bridge the gap between emerging technologies and their application to cancer communications. NCI coordinates activities with the World Wide Web Consortium on Cancer to collaborate, share information, and support one another in the delivery of authoritative cancer knowledge via survivor-run and other Web sites. We have arrangements with commercial online vendors to provide their customers information on NCI resources, publications, and the CIS hotline (1-800-4CANCER). NCI is working with an Internet access hardware and software provider to enable low income families to add cancer information to their Web portal. In addition, we are collaborating with a maker of novel devices for inexpensive Internet access to include links to NCI and to customize for use by cancer patients.

In 2000, NCI established the **Eleanor Nealon Extraordinary Communicators Lecture Series**, which pays tribute to outstanding communicators who have advanced the science of communication or the communication of science. NCI also has supported several creative **meetings and workshops on cancer and health communications-related topics**, including a Media and Health Education workshop (co-sponsored with Rutgers University), the Future of Health Technology Summit 2000 (co-sponsored with the Massachusetts Institute of Technology), and the Strategic Education and Training in Health Communication workshop.

NCI reorganized its **Office of Communications** in May 2000 to provide a comprehensive, integrated, and technology-based communication structure that will increase the effectiveness of our interactions with the public. New organizational units will enhance our capabilities in Web design and evaluation, maximize our use of emerging technologies, optimize our ability to help people with cancer inquiries navigate through the NCI communications structure, and increase our readiness to form partnerships with outside organizations. A new **Office of Education** also has been established as an essential NCI communication arm.

For more information on NCI's Cancer Communications initiatives, go to dccps.nci.nih.gov/eocc or cancer.gov/initiatives.

Budget Increase Request for 2002 Cancer Communications

1. Support cancer communications planning, research, evaluation, dissemination, and marketing.	\$3.5 M
2. Create Centers of Excellence in Cancer Communications Research.	12.0 M
3. Develop a menu of communication choices.	6.0 M
4. Train health communications scientists, researchers, and practitioners.	3.0 M
5. Continue to integrate and restructure NCI's communications activities.	2.0 M
Management and Support	1.0 M
Total	\$27.5 M

The Changing Scene for Cancer Communications

Changes in the role and accessibility of information are altering health care practices, patient-physician relationships, and the way consumers and patients acquire and use information. Where once physicians were the main source of health information, now many consumers are actively using a variety of information sources to meet their needs. Both consumers and health professionals now have an array of new opportunities for creating, distributing, and acquiring health information from sources such as the World Wide Web, electronic mail, individually tailored print and multimedia materials, interactive computer games, interactive kiosks, and wireless pagers.

These “new media” already have had an enormous impact:

- According to a poll released by Harris Interactive in February 2000, more than half of U.S. households are now online and of these, 90% use the Internet.
- ACNielsen reported in May 2000 that nearly two-thirds of Americans over age 12 have access to the Internet, and half go online every day.
- A 1999 Harris Poll found that approximately 70 million (74 percent) of adults who use the Internet searched online for health information. Cancer was the third most sought-after health topic.
- In 1999, cancer-related listservs (e-mail groups devoted to a specific topic) hosted by the Association of Cancer Online Resources processed 1.9 million pieces of e-mail each week.

Substantial barriers still prevent major segments of the population from seeking and/or using cancer information. Some people continue to lack access to the array of cancer communications media. Others are faced with content that is unintelligible to them (in the wrong language or in language that is too complex), culturally inappropriate, or simply ineffective. There clearly is a “digital divide” in our Nation and around the world. Those who lack access to information and new online tools – the information “have nots” – are more likely to be poor, to have less than a high

school education, and to be ethnic minorities. We must work to eliminate this divide. How can we promote knowledge about, tools for, access to, and use of cancer information, given the high national rates of medical illiteracy? How can we ensure that cancer communications and interventions are relevant, meaningful, and culturally sensitive to diverse audiences? How can we know what does not work and why? We are challenged to help physicians and other health care providers optimize their communications about cancer, and to redesign information systems so they give people the information they want how, when, and where they want it.

New information technologies must complement, not replace, older but effective strategies, such as the mass media, one-to-one counseling, and targeted print communications. For example, most people still want to talk directly with a knowledgeable and supportive person. Such interactions can enhance outcomes of and satisfaction with care. As we develop new technologies, we must not lose sight of the importance of personal interactions and the need for continuing research and practice to strengthen one-to-one communications. We also must take into account that consumers, patients, and health professionals alike are coming to expect seamless, integrated, accessible, tailored communication choices. They want to move easily among these new and older information technologies – for example, to go from a Cancer Information Service (CIS) information specialist to CancerNet or to talk to the specialist while viewing a Web site.

To be effective, cancer communications must be integrated into the cancer continuum from prevention through treatment to survivorship and to end-of-life issues, including palliative care and pain management. Communication should be an integral component of quality cancer care for all, regardless of race, ethnicity, health status, education, income, age, gender, or geographic region.

“Science and communications are always inextricably entwined. From research to the patient, the imperative to communicate deepens. Communication empowers, enlightens, soothes, clarifies life and death...”

— Dr. Richard Klausner

Planning National Agendas in Disease-Specific Research

Reports on the toll that cancer places on the American people are overwhelming. 1.2 million new cases diagnosed in 2000. A half million people dead this year. Nine million with a history of cancer right now. But these daunting statistics fail to communicate the tremendous burden borne by patients, families, and friends who want to better understand and deal with a specific form of cancer.

Five years ago, NCI instituted a comprehensive, dynamic planning process that incorporated three separate – but equally vital – elements. The first of these focuses on our continuing efforts to support scientific discovery and application of discovery to human health – a range of programs that currently form the basis for the “Challenge” section of this document. The second involves investment in areas of research that are broadly applicable to all cancers, as discussed in this document’s “Extraordinary Opportunities” section. The third element of our process is disease-based planning.

When NCI began its new approach to planning, we first identified the broadly applicable scientific opportunities through which vital progress could be made most quickly. We then began a comprehensive review of the large programs that support discovery. Once these assessments were well underway, we stepped back and asked ourselves, “Can these broad investments be tailored to specific cancers? Have we developed the tools and infrastructure to conduct disease-specific research, and to do it well? Have we defined those broad-based research areas that can best support our disease-specific efforts?” Our efforts to answer these questions culminated in the creation of a new vehicle for planning disease-specific research: the Progress Review Group.

PRGs: THE PEOPLE, THE PROCESS, THE PLAN

Progress Review Groups (PRGs) are panels of 20-30 experts that are convened to develop a national research framework for individual types of cancer. The PRGs assess the state of the science, identify gaps in knowledge and barriers to progress, and identify research priorities. Beginning with an assessment of the NCI’s current research portfolio, the members of each PRG identify and prioritize future research areas for the particular cancer under study, and summarize their deliberations in a written report.

Each PRG is given a compelling charge: *To imagine and build the future.* In doing so, the groups engage the scientific, medical, and advocacy communities in a dialogue on potential directions for

Schedule of Completed and Planned Progress Review Groups

Completed August 1998	Breast Cancer
Completed August 1998	Prostate Cancer
June 1999 - November 2000	Colorectal Cancer
November 1999 - February 2001	Brain Tumors
February 2000 - May 2001	Pancreatic Cancer
April 2000 - August 2001	Leukemia-Lymphoma-Myeloma
August 2000 - November 2001	Lung Cancer
December 2000 - February 2002	Gynecologic Cancers
March 2001 - May 2002	Kidney/Bladder Cancer
June 2001 - August 2002	Stomach/ Esophageal Cancer
September 2001 - November 2002	Liver/Bile Duct Cancer
December 2001 - February 2003	Skin Cancers

research. In spotlighting the gaps in our knowledge, and recommending how those gaps can be filled, the PRGs give NCI the tools it needs to build the future and kindle the interest of the best scientific minds in research on specific cancers.

The PRG process is intensive and extends over a number of months. To date, PRGs have been completed for breast, prostate, and colorectal cancers. A Brain Tumor PRG, conducted in collaboration with the National Institute of Neurological Disorders and Stroke, is nearing completion. PRGs for all of the other most common types of cancer are planned through 2002; ongoing and planned PRGs are outlined in the chart on page 96.

OUR COMMITMENT: WE WILL LISTEN AND WE WILL ACT

NCI is committed to responding rapidly and enthusiastically to recommendations from the Progress Review Groups. For each PRG, we:

- Determine to what extent the PRG's recommendations are being addressed or could be addressed by existing programs or efforts.
- Develop an implementation plan for the recommendations and discuss that plan with the members of the PRG.
- Communicate our plans to the scientific community, and enlist their active participation in the implementation process.
- Track progress toward goals and report on the results.

Based on PRG recommendations, NCI may modify existing programs or activities, or create new ones. For example, the Breast Cancer PRG noted that our lack of understanding of the biology and developmental genetics of the normal breast was a significant barrier to progress against the disease. NCI responded by releasing a Program Announcement, in conjunction with several other NIH Institutes, seeking applications for research on normal breast development, as well as on changes in the breast throughout the progression of early and advanced cancer.

NCI also responds to the findings and recommendations of Progress Review Groups in other ways. Proposed research projects that address prior-

The Common Scientific Outline

"What research are you doing on prostate cancer?" "How much of your funding for basic research is focused on prevention?" These are common questions, but they can be surprisingly difficult to answer.

In order to arrive at the answers to these questions, planners and policy makers must have the necessary information readily at hand. To respond to this need, the NCI developed a new coding system to categorize its research simply and systematically, by type of cancer and area of science. This new coding system, known as the Common Scientific Outline (CSO), grew out of the NCI's experience with PRGs and disease-specific task forces over the last several years and has been developed in conjunction with the Department of Defense (DOD) U.S. Army Medical Research and Materiel Command because of its work in cancer research.

Both NCI and DOD have now used the CSO to categorize their research projects for Fiscal Years 1997-1999. In addition, several national and international organizations – both public and private – have been invited to participate in a pilot project to use the CSO to classify and analyze their research portfolios.

Because of the simplicity and accessibility of its design, the CSO and the reporting and analysis tools it makes possible are likely to have an impact on shaping disease-related research and scientific planning. The CSO will also foster coordination between NCI, DOD, and other organizations that support cancer research by identifying gaps in funding.

ities identified by PRGs but rank just below the cut-off for funding receive special consideration in the funding exceptions process.

WHAT WE ARE LEARNING

With reports from three Progress Review Groups completed, and several more underway, NCI has begun to take stock of its efforts to support disease-specific research. The results to date have been encouraging. About 80 percent of the recommendations resulting from PRGs to date can be addressed by programs that are already in place or with minor modifications to existing programs. In fact, there are core scientific needs – for example, the need for research training, or for the development of disease biomarkers – that appear to be universal, regardless of the disease. Many of the remaining recommendations represent genuine gaps in research or infrastructure that NCI must and will address. A few of these, however, fall outside the Institute’s purview (e.g., Medicare reform), and NCI’s response to these recommendations will

necessarily involve advising other organizations or agencies, rather than acting directly.

These results indicate to us that we are on the right track. But the larger question that remains is whether this approach to disease-based research planning makes a difference in research and discovery over the long term. To that end, we are beginning to develop a plan for evaluating the PRG process and outcomes, and we are exploring strategies to reassess diseases that remain areas of high concern. Starting with the Breast and Prostate PRGs, we will analyze changes in funding levels, types of research funded, and grant application response that occur after the completion of a PRG. We will issue a status report two to three years after each PRG, and the members will reconvene to discuss the status of the recommendations and NCI’s response and to recommend further action. This process will be in place by 2001, and will provide valuable information and insight about our directions in disease-based planning.

For NCI Progress Review reports and schedules, go to planning.cancer.gov.

“There’s So Much More We Can Do”

A Talk with a PRG Co-Chair

Harold Moses, M.D., is Director of the Vanderbilt Cancer Center in Nashville. In 1998, he served as Co-Chair of NCI’s Breast Cancer Progress Review Group. Recently, we talked to Dr. Moses about the PRG and the future of breast cancer research.

Why do we need Progress Review Groups?

PRGs allow us to convene a group with diverse backgrounds to step back and take a look at where we are, and to speculate on where we should be going in cancer research for maximum benefit. PRGs also serve to show Congress and the public that NCI really does have a reasonable planning process, and they indicate directions for future research.

This attracted me to the process when Dr. Klausner asked me to serve as Co-Chair. It looked like chairing the PRG would be fun, and it seemed that through the process, we might come out with broad recommendations for breast cancer research funding.

What is realistic to expect from the PRG process? What are its limitations?

It’s realistic to expect PRGs to give a picture of where the research is now, and a broad outline of where it should be going. PRGs are also good for identifying areas of critical need.

In terms of limitations the PRGs can only give a “snapshot in time” of the state of the science, or of research needs, or of exciting opportunities. Things change. The danger would be if the NCI tried to adhere too rigorously to a plan made in the past. A PRG report is like any strategic plan – it’s a work in progress that needs to be modified continuously to address changing opportunities and needs.

Looking specifically at the Breast Cancer PRG, what do you consider to be the most valuable things to come out of the process?

Well, it's difficult to place a value judgment on this. But the realization of how little we know about the basic biology of the mammary gland, and about the progression of cancer from normal to precancer through metastasis, was certainly very important. The group recognized how important an understanding of normal breast biology would be to designing clinical trials, as well as identifying surrogate endpoints and markers for studies of all kinds, including epidemiologic and prevention studies.

While the Breast Cancer PRG was going on, NCI had many other ongoing working groups, and they were making similar recommendations. It's amazing how similar the recommendations coming out of the breast group were to those coming out of the Prostate PRG, for example. So the recommendations we were coming up with were not necessarily unique to breast cancer, but they were critical to the advancement of science in a number of areas.

Are you satisfied with NCI's response to the PRG's recommendations?

I was absolutely amazed at NCI's response; it was fantastic, in my view. Some of the most exciting aspects of NCI's response, to me, include the increased funding for investigator-initiated grants, especially those in basic biology and early progression; the renewed emphasis on mouse models; and the CGAP [Cancer Genome Anatomy Project] movement to incorporate some of our recommendations, such as the development of gene expression profiles for normal breast tissue in addition to breast cancer.

What did the Breast Cancer PRG reveal about the current state of breast cancer research?

It showed us that we've come a long way relative to five or ten years ago. We've made enormous advances, and that includes advances in basic science that are applicable to all types of cancer. It's now becoming clear in the survival rates that breast cancer can be more of a chronic disease, not a disease that is invariably fatal.

Another thing that came out of this group was the critical importance of basic research to progress in breast cancer, and the recognition of its importance to all the groups at the table – basic scientists, clinicians, epidemiologists, prevention researchers, and so on. PRG members in all of those disciplines recognized the urgent need for advances in basic research.

What would you like to see happen in the future in breast cancer research?

I would like to see us figure out better preventive measures against breast cancer, as well as treatments that will cure the disease with minimal side effects. A major need is to figure out how to do Phase II clinical trials more quickly and efficiently. There are so many amazing treatment agents in the pipeline B targeted agents with very low toxicity. Figuring out how to use those in the most appropriate way is a major challenge.

We also need better diagnostic criteria. We need to know which pathways are altered in precancer, early cancer, metastatic cancer. In addition, we need to keep plugging along in normal biology.

What I would foresee is that someday, we'll be able to get the gene expression profile for each individual cancer, then administer a treatment that's targeted to that cancer at the molecular level, likely in combination with a standard treatment. It's unlikely that any single treatment will be effective against all breast cancers.

There are a lot of opportunities right now in breast cancer research, but they involve a lot of work. It's exciting; there have been many important accomplishments – there's so much more we can do.

How It All Comes Together

The programs and initiatives described in this document promise to one day increase our understanding of cancer and improve the options available to patients, their families, and the physicians who care for them. Examining how these challenges and opportunities apply to lung cancer – the leading cause of cancer death in the United States – illustrates the potential they hold for improving our ability to prevent, detect and diagnose, and treat cancer in all its forms.

Prevention

In one of many efforts to respond to the challenge of studying emerging trends in cancer (page 38), detailed maps are developed to display data on cancer deaths in the Atlas of Cancer Mortality. Researchers use these data to identify previously unrecognized geographic patterns in cancer mortality and formulate hypotheses for further research. A few years ago, investigators using the atlas observed that men living along the Southeast coast of the United States were dying of lung cancer at unusually high rates. Follow-up investigation led to the discovery that many of these men had been exposed to asbestos while working in the shipyards during World War II, a key piece of evidence linking asbestos to lung cancer and the need to prevent future exposures to asbestos.

As a result of the extraordinary opportunities identified for research on genes and the environment (page 64) and tobacco and tobacco-related cancers (page 86), scientists are turning their attention to the perplexing question of why some individuals exposed to cancer-causing agents develop lung cancer while others do not. Researchers are beginning to find the answers by combining genetics and epidemiology to examine the relative roles of genes, smoking, and other environmental and lifestyle factors in lung cancer development.

Through the extraordinary opportunity for cancer communications (page 91), we hope to find the best ways to tailor and target prevention messages about smoking and other risk factors for lung cancer to teens, adults, or health care providers. These communications must give special attention to the distinct smoking patterns and preferences of different racial and ethnic groups. For example, African American smokers are more likely than others to choose menthol cigarettes, a preference that may inadvertently result in the absorption of higher levels of toxic substances from tobacco smoke.

Detection and Diagnosis

Investigators pursuing the extraordinary opportunity for research on the signatures of cancer cells (page 74) are focused on learning as much as possible about the unique characteristics of normal cells and the changes that occur when a normal cell becomes cancerous. As scientists identify and catalog the molecular changes that accompany different types and stages of cancer, they may one day be able – through a simple test of body fluid or cells – to use these biomarkers as tools to detect and diagnose lung cancer at its earliest stages. For example, now that we know that lung cancer development is accompanied by alterations in the cells that line the bronchial passages, investigators are closer to finding an accurate and reliable biomarker for early detection of lung cancer.

Because only 15 percent of lung cancers are diagnosed in the early stages when they are most curable, a reliable, cost-effective tool for screening could considerably increase the chances of successful treatment. Through NCI's national clinical trials program (page 33), researchers pursuing the extraordinary opportunity for cancer imaging (page 69) are evaluating the use of spiral computed tomography (CT) for early detection of lung cancer. They are trying to determine whether this relatively new imaging technology detects more cases of lung cancer than chest x-rays and whether its use will ultimately save lives.

Treatment

Eventually, we hope that what we learn about molecular signatures can be applied, through the extraordinary opportunity for research on molecular targets of prevention and treatment (page 80), to develop therapies targeted for maximum benefit in treating lung cancer.

Currently, three Specialized Programs of Research Excellence (page 31) are dedicated to developing and evaluating new treatments for lung cancer. They bring teams of scientists together in interdisciplinary research centers to focus on specific cancers and hasten the movement of research findings from the laboratory to the clinic.

Next Steps

NCI will convene a Progress Review Group in the fall of 2000 to assess the state of the science in lung cancer, identify gaps in knowledge and barriers to progress, and rank research priorities for lung cancer-related research. (See page 96.) The report from this group is expected to guide our lung cancer research for years to come.

Valuable World Wide Web Locations

Users can access all of the following from the **NCI Home Page** at cancer.gov.

Go to:	For:
CancerNet™ at cancernet.nci.nih.gov	Cancer information for patients and physicians, including links to the Physician Data Query (PDQ®) and CANCERLIT® databases.
cancerTrials at cancertrials.nci.nih.gov	Information about clinical trials for patients, physicians, and investigators.
Extraordinary Opportunity Initiatives at cancer.gov/initiatives	Details on the NCI initiatives related to the extraordinary opportunities for investment described in this document.
NCI Funding Opportunities at deainfo.nci.nih.gov	Information on grants, contracts, and other forms of research funding available through NCI.
NCI Research Resources at cancer.gov/resources	A directory of over 100 research services and tools for cancer researchers.
Cancer Research Training at cancertraining.nci.nih.gov	Information on research training, career development, and educational opportunities available through the NCI.
Cancer Centers at cancer.gov/cancercenters	Information about the Cancer Centers Program, including links to NCI's national network of Cancer Centers.
SEER Web site at www-seer.cancer.gov	The most authoritative information on cancer incidence and survival in the United States provided by the NCI Surveillance, Epidemiology, and End Results (SEER) program.
<i>Atlas of Cancer Mortality</i> at cancer.gov/atlas	Maps, text, tables and figures on cancer death rates in the U. S. 1950-1994 for about 40 cancers. Includes customizing capability.
Cell Biology and Cancer at http://science-education.nih.gov/nihhtml/colsupp/nci-cell	An introduction to the biology of cancer for high school students and others.

Information by Telephone 1-800-4-CANCER (1-800-422-6237)

The Cancer Information Service national telephone hotline at 1-800-4-CANCER provides confidential information, in English or Spanish, on all aspects of cancer, including prevention, treatment and clinical trials. Physicians and other health professionals can call 1-800-345-3300 to make requests for CancerNet Search Services to obtain PDQ and CANCERLIT information.

Electronic Mail Services

Send an email to cancermail@icic.nci.nih.gov with the one-word message "Help" to receive a contents list and ordering instructions for receiving NCI information via email. Physicians and other health professionals can send an email to pdqsearch@icic.nic.nih.gov to request CancerNet Search Service for PDQ and CANCERLIT information.

To receive information by fax, call 1-800-624-2511 from a touch-tone phone or fax machine hand set and follow recorded instructions to receive a CancerFax® contents list.

Print Publications

Over 600 publications and audiovisual materials, many published in Spanish, are available from NCI. Telephone the **1-800-4-CANCER** service or order online from the CancerNet site at cancernet.nci.nih.gov.

This Document

Additional copies of this document can be ordered by e-mail at cisocc@nih.gov, by phone at 1-800-4-CANCER, or by fax at 301-330-7968. This document, with additional information and links to related information and previous plan and budget proposals, is online at plan2002.cancer.gov.



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Extraordinary Opportunity and NCI Challenge Champions

Dr. Richard Klausner served as Editor-in-Chief. Several NCI staff members served as "champions" for the Extraordinary Opportunity and NCI Challenge areas. They developed the goals, plans, and resource requirements for their areas and worked with OSPA staff to develop the background narrative.

Extraordinary Opportunity Champions

Genes and the Environment –
Dr. Robert Hiatt, *Dr. Robert Hoover*,
Dr. Kenneth Buetow
Cancer Imaging – *Dr. Ellen Feigal**,
Dr. Daniel Sullivan
Defining the Signatures of Cancer Cells –
Dr. Robert Strausberg, *Dr. Dinah Singer*
Molecular Targets of Prevention and
Treatment – *Dr. Robert Wittes*,
Dr. Edward Sausville
Research on Tobacco and Tobacco-Related
Cancers – *Dr. Robert Croyle*,
Dr. Neil Caporaso
Cancer Communications –
Dr. Barbara Rimer, *Dr. Susan Sieber*
NCI Challenge Champions
Investigator-Initiated Research –
Dr. Marvin Kalt
Centers, Networks, and Consortia –
Dr. Ellen Feigal, *Dr. Brian Kimes*
National Clinical Trials Program –
Dr. Robert Wittes, *Dr. Michaele Christian*
Studying Emerging Trends in Cancer –
Dr. Rachel Ballard-Barbash,
Dr. Brenda Edwards
Quality of Cancer Care –
Dr. Joseph Lipscomb, *Dr. Martin Brown*
Reducing Cancer-Related Health
Disparities – *Dr. Robert Hiatt*,
Dr. Jon Kerner
Informatics and Information Flow –
Dr. John Silva, *Ms. MaryAnn Guerra*
Training, Education, and Career
Development – *Dr. Brian Kimes*

In addition to these Champions,
Dr. Joseph Fraumeni, *Ms. Jill Johnson*,
*Dr. Barry Kramer**, *Ms. Mary McCabe*,
and *Ms. Susan Waldrop* made significant
contributions to the content and accuracy
of this document.

Fiscal Year 2002 Planning Committee

Members of this committee helped to ensure that this document clearly and accurately describes the excitement and promise of NCI's efforts, our needs and plans, and the vision for the future of our research programs.

Dr. Richard Klausner
Director, NCI

Dr. Alan Rabson
Deputy Director, NCI

Dr. Robert Wittes
Deputy Director, Extramural Science and
Director, Division of Cancer Treatment and
Diagnosis

*Dr. Carl Barrett**
Director, Division of Basic Sciences

*Dr. Joseph Fraumeni**
Director, Division of Cancer Epidemiology
and Genetics

Dr. Peter Greenwald
Director, Division of Cancer Prevention

Ms. MaryAnn Guerra
Director, Office of Management

Dr. Joseph Harford
Associate Director, Special Projects

*Mr. John Hartinger**
Associate Director, Financial Management

Dr. Marvin Kalt
Director, Division of Extramural Activities

*Dr. Edison Liu**
Director, Division of Clinical Sciences

Dr. Suresh Mohla, Chair
Extramural Advisory Board

Ms. Cherie Nichols
Director, Office of Science Planning and
Assessment

*Dr. Barbara Rimer**
Director, Division of Cancer Control and
Population Sciences

*Dr. Susan Sieber**
Director, Office of Communications

*Dr. Dinah Singer**
Director, Division of Cancer Biology

*Ms. Susan Waldrop**
Director, Office of Science Opportunities

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Director's Consumer Liaison Group

Dr. Phillip Sharp, Chair
Ms. Ellen Stovall, Member
National Cancer Advisory Board

*Editorial Board member