National Cancer Institute

The NCI Strategic Plan

for Leading the Nation

To Eliminate the Suffering and Death Due to Cancer

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

NCI Senior Leadership: Andrew C. von Eschenbach, Anna Barker, Mark Clanton, John Niederhuber, Ken Buetow, Bob Croyle, Jim Doroshow, Greg Downing, Joe Fraumeni, Harold Freeman, Paulette Gray, Peter Greenwald, John Hartinger, Alan Rabson, Dinah Singer, Dan Sullivan, Bob Wiltrout **Office of Science Planning and Assessment:** Cherie Nichols, Kathie Reed, Marianne Kost, Anna Levy, Samir Sauma, Lisa Stevens, Kevin Wright, Anne Tatem, Kevin Callahan, Buddy Clark, Jim Corrigan, Denise Crouse, Norma Davis, Rabiah Hendricks, Laurencia Hutton, D. J. Joya, Mary Leveck, Kate McNeill, Genevieve Medley, Christine Moretto **Strategy Development Teams:** Understanding the Causes and Mechanisms of Cancer Team Bob Hoover, Trisha Hartge, Nat Rothman, Stephen Chanock, Peggy Tucker, Cathy McClave, Dan Gallahan, Suresh Mohla, John Sogn, Curt Harris, Stuart Yuspa, Doug Lowy, Snorri Thorgeirsson, Mimi Poirier, Carl Wu, Jim Jacobson, Vernon Steele, Joe Tangrea, Sharon Ross, Levy Kopelovich, Ed Trapido, Debbie Winn, Ken Chu, Samir Sauma Accelerating Progress in Cancer Prevention Team Howard Parnes, Doug Weed, John Milner, Gary Kelloff, Carol Macleod, Shelia Prindiville, Nancy Colburn, Steve Libutti, Regina Ziegler, Jon Kerner, Cathy Backinger, Emmanuel Taylor, Jill Bartholomew, Anne Tatem Improving Early Detection and Diagnosis Team Sudhir Srivastava, Phil Prorok, Jacob Kagan, Guillermo Marquez, Neeraja Sathyamoorthy, Grace Ault, Betsy Read-Connole, Louis Staudt, Elise Kohn, Elaine Jaffe, Richard Alexander, Steven Rosenberg, Jeff Strathern, Pete Choyke, Sriram Subramaniam, Gordon Whiteley, Helen Meissner, Mukesh Verma, Sheila Taube, Kenneth Bielat, Barbara Wingrove, Rose Mary Padberg, Lisa Stevens Developing Effective and Efficient Treatments Team Michaele Christian, Jill Johnson, Gary Becker, Lee Helman, Jeff Schlom, Crystal Mackall, Allan Weissman, Cheryl Marks, Richard Cumberlin, Jim Crowell, Karen Johnson, Martin Brown, Travis Earles, Kevin Wright Understanding the Factors that Influence Cancer Outcomes Team Nada Vydelingum, Lois Travis, Meryl Sufian, Steve Clauser, Suzanne Heurtin-Roberts, Ted Trimble, Anita Ousley, Anna Levy Improving Quality of Care and Quality of Life Team Julia Rowland, Neeraj Arora, Molla Donaldson, Ann O'Mara, Ted Trimble, Norm Coleman, Jeff Rubin, Jim Mitchell, Peter Blumberg, Roland Garcia, Andrea Denicoff, Elizabeth Neilson, Marianne Kost Overcoming Cancer Health Disparities Team Jane Daye, Leslie Cooper, Pebbles Fagan, Sabra Woolley, Worta McCaskill-Stevens, Terri Cornelison, Linda Brown, Caryn Steakley, Martin Gutierrez, Frank Govern, Ted Trimble, Rochelle Rollins, Lenora Johnson, Sanya Springfield, James Hadley, Denise Crouse **NCI Planning Contacts:** Jill Bartholomew, Christina Bruce, Lynn Cave, Jane Daye, Andrea Denicoff, Jim Dickens, Travis Earles, Brooke Hamilton, Chris Hatch, Marianne Henderson, Maureen Johnson, Jackie Lavigne, Peggy Rhoades, Kathleen Schlom, Jennifer Sienko, Kara Smigel-Croker, Stacey Vandor, Linda Weiss, Jeff White, Steve White, Mark Alexander, Bryan Baker, Tai Baker,

Director's Message

Early in 2003, as the Director of the National Cancer Institute, I announced our Challenge to the Nation—to eliminate the suffering and death due to cancer by 2015. I have been extraordinarily pleased with the response of the cancer community and the desire of many to partner with us to make it happen. This Challenge has become the Vision for the Nation's Cancer Program as we all strive to dramatically reduce the burden of cancer. NCI has a clear mandate and responsibility to lead the pursuit of fundamental scientific knowledge and support the cancer community by providing the funding, infrastructure, tools, and other resources necessary to make this Vision a reality.

By maintaining a clear focus on our purpose, we will build synergy around a seamless, integrated, and continuous discovery, development, and delivery process. Our research will be targeted to those areas of pursuit that show greatest promise. New development will promote the most compelling interventions based on evidence emerging from that discovery. The delivery of evidence-based interventions will be universal. What we learn in public health and medical practice will foster our understanding of the biology of cancer and make possible increasingly more effective interventions.

This Plan sets forth a framework within which NCI can lead and work with others to address some of the most perplexing challenges of cancer. It has been conceived by NCI leadership and staff with ongoing input from our NCI advisory groups and regular interactions with the cancer research and advocacy communities.

We hope that our NCI Strategic Plan will serve as a guide for decision making both at NCI and across the cancer community. The Plan will only be of value when it is used to formulate integrated and deliberate solutions to the cancer problem. We believe that the Vision is within our grasp, and we are prepared to stretch the boundaries of science, imagination, and human will to achieve it.

Andrew C. von Eschenbach
January 2006

After many years with only a macroscopic view of cancer followed by years of being able to see it only through a microscope, scientists are now able to work from a molecular view. Never before have so many scientific tools and so much biomedical knowledge been assembled to power our ability to reach our Vision to eliminate the suffering and death due to cancer by 2015. We as a Nation will achieve this Vision by optimizing new approaches in interdisciplinary collaboration and transdisciplinary science and by applying proven interventions in basic science, medical practice, public health programs, and policy.

As leader of the National Cancer Program, the National Cancer Institute (NCI) will continue to provide vision and leadership to the nationwide community of researchers, public health workers, healthcare providers, patients, advocates, and policymakers working to defeat cancer. This Strategic Plan outlines what we believe NCI must do. It includes continued work in broad research areas and optimal use of existing and new knowledge to develop and apply evidence-based interventions for preventing and controlling all cancers. Our success will depend on our ability to integrate our activities across a seamless continuum of discovery, development, and delivery; partner with others to leverage resources and build synergy; and ensure that what we learn in the clinic and community transforms future discovery.

This document will serve as a reference and guide for the development of operational level plans and an organizer for measuring and reporting progress. We will continue to use *The Nation's Investment in Cancer Research* as NCI's annual operational plan and budget where we outline milestones for the fiscal year and provide more specificity as to how we will carry out the objectives described in this Strategic Plan. In all of our planning, we will endeavor to be responsive to changing public health needs and to the scientific and technological opportunities that come our way.

Our Vision

A Nation free from the suffering and death due to cancer by 2015 with dramatic reductions in cancer incidence.

Our Mission

Reduce the burden and eliminate the adverse outcomes of cancer by leading an integrated effort to advance fundamental knowledge about cancer across a dynamic continuum of discovery, development, and delivery.

National Cancer Institute
Leading the Nation

THE FRAMEWORK TO ELIMINATE THE SUFFERING AND DEATH DUE TO CANCER BY 2015

To create a Nation free from the suffering and death due to cancer with dramatic reductions in cancer incidence.

VISION

MISSION

Reduce the burden and eliminate the adverse outcomes of cancer by leading an integrated effort to advance fundamental knowledge about cancer across a dynamic continuum of discovery, development, and delivery.

TO PREEMPT CANCER AT EVERY OPPORTUNITY

> Understand the Causes and Mechanisms of Cancer
> Accelerate Progress in Cancer Prevention
> Improve Early Detection and Diagnosis
> Develop Effective and Efficient Treatments

TO ENSURE THE BEST OUTCOMES FOR ALL

> Understand the Factors that Influence Cancer Outcomes
> Improve the Quality of Cancer Care
> Improve the Quality of Life for Cancer Patients, Survivors, and Their Families
> Overcome Cancer Health Disparities

KEY PARTNERS IN REALIZING THE VISION

> Advisory Groups
> Advocates
> Cancer Researchers
> Government Leaders
> Patients
> President and Congress
> Professional Societies
> Public

A Nation free from the suffering and death due to cancer.

Leading the Nation to Eliminate the Suffering and Death Due to Cancer

Our Strategic Objectives

To Preempt Cancer at Every Opportunity

We will conduct and support basic, clinical, and population research to gain a more complete understanding of the genetic, epigenetic, environmental, behavioral, and sociocultural determinants of cancer and the biological mechanisms underlying cancer resistance, susceptibility, initiation, regression, progression, and recurrence.

We will accelerate the discovery, development, and delivery of cancer prevention interventions by investing in research focused on systems biology, behavior modifications, environmental and policy influences, medical and nutritional approaches, and training and education for research and health professionals.

We will support the development and dissemination of interventions to detect and diagnose early-stage malignancy.

We will support the development and dissemination of interventions to treat malignancy by either destroying all cancer cells or modulating and controlling metastasis, both with minimal harm to healthy tissue.

To Ensure the Best Outcomes for All

We will support and conduct studies to increase our understanding of and ability to measure the environmental, behavioral, sociocultural, and economic influences that affect the quality of cancer care, survivorship, and health disparities.

We will support the development and dissemination of quality improvement interventions and measure their success in improving health-related outcomes across the cancer continuum.

We will support the development and dissemination of interventions to reduce the adverse effects of cancer diagnosis and treatment and improve health-related outcomes for cancer patients, survivors, and their families.

We will study and identify factors contributing to disparities, develop culturally appropriate intervention approaches, and disseminate interventions to overcome those disparities across the cancer control continuum from disease prevention to end-of-life care.

To preempt cancer at every opportunity, we will work to:

1. Understand the Causes and Mechanisms of Cancer

2. Accelerate Progress in Cancer Prevention

3. Improve Early Detection and Diagnosis

4. Develop Effective and Efficient Treatments

NCI will continue scientific discovery into the genetic, molecular, and cellular determinants of cancer susceptibility and initiation and support studies to better understand risk reduction, prevention, early detection, diagnosis, and treatment. We will use research results to develop individualized approaches for preempting the initiation and progression of cancer at every stage, from precancer through metastasis. We will define optimal strategies for dissemination and delivery in a context that will transform public health. We will work collaboratively with providers to focus on prevention as our first line of defense. Accelerated discovery will generate new information about cancer at the genetic, cellular, individual and population levels. Our ever-increasing understanding of the abnormalities involved in the onset and progression of cancer will provide the targets that will help us develop personalized, integrated, and evidence-based interventions.

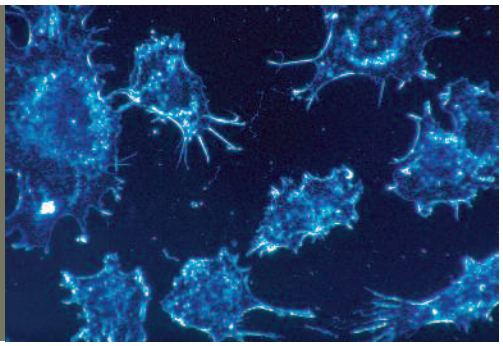
To Preempt Cancer at Every Opportunity

STRATEGIC OBJECTIVE 1

Understand the Causes and Mechanisms of Cancer

We will conduct and support basic, clinical, and population research to gain a more complete understanding of the genetic, epigenetic[1], environmental, behavioral, and sociocultural determinants of cancer and the biological mechanisms underlying cancer resistance, susceptibility, initiation, regression, progression, and recurrence.

Cancer is a complex set of diseases that must be understood from multiple perspectives. Research that improves our understanding of its causes and mechanisms—from assessing cancer risk to elucidating the process of metastasis—is essential to our ability to develop and apply interventions to preempt cancer initiation and progression. NCI's plan for deciphering the causes and mechanisms of cancer includes continued support of consortial studies in molecular epidemiology to assess complex risk factors, research on the tumor macroenvironment and microenvironment, research on the role of altered gene expression in cancer progression, and characterization of the roles of susceptibility genes in cancer risk and initiation. We will continue to foster a systems approach to cancer research, apply advanced technologies in diverse research settings, and elucidate the relationship between cancer and other diseases. We will continue to support both investigator-initiated research and large, directed interdisciplinary and multidisciplinary programs as a comprehensive strategy to unravel the components and complexities of multiple risk factors for cancer, understand specific types of cancer based on their molecular characteristics, and develop rationally designed interventions to prevent, detect, diagnose, and treat cancer and to predict patient response to therapy.



[1] Pertaining to the approximately stepwise process by which genetic information, as modified by environmental influences, is translated into the substance and behavior of an organism.

STRATEGY 1.1 — Gain a full understanding of genetic susceptibility and cancer causation.

New approaches to genetic profiling are revealing a complex spectrum of cancer related genetic variation among individuals, ranging from highly penetrant but uncommon alleles to common polymorphisms that exert subtle but key effects. NCI will:

- Support initiatives to investigate the underlying basis of the full spectrum of genetic susceptibility to cancer.
- Sustain investigations of individuals with known mutations in high penetrance cancer susceptibility genes to uncover the earliest molecular aberrations underlying the carcinogenic process.
- Continue studies of cancer prone families that carry susceptibility genes known to increase the risk of developing related tumors, such as breast, ovarian, and endometrial tumors. This research will reveal how abnormalities in cancer susceptibility genes lead to varying cancer outcomes.
- Support comparison of biomarker panels across various malignancies to characterize the role of mutations of any penetrance in common critical pathways, such as those associated with inflammation, repair, immunity, growth, obesity, and metabolism.
- Facilitate the use of whole genome scans in population studies to identify lower penetrance cancer susceptibility genes that contribute to cancer development through their interaction with environmental factors and other genes.

Taken together, this research will generate unprecedented volumes of data for the molecular characterization of tumors, the identification of molecular predictors of cancer, and the characterization of fundamental similarities among malignancies. Analysis of this data will lead to the identification of molecular targets for cancer prevention and early detection, and the development of patient-specific approaches to cancer prognosis and treatment.

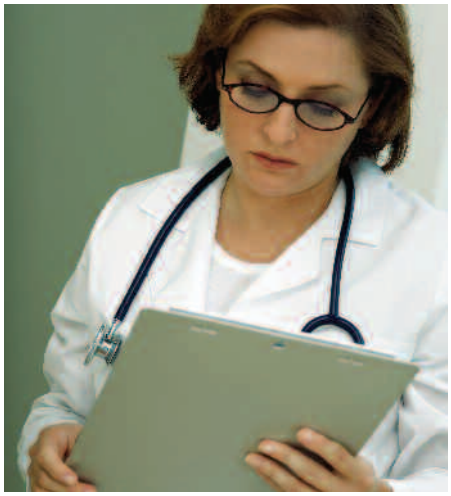
STRATEGY 1.2 — Identify and characterize the influence of the macroenvironment on the chain of events that leads to cancer and its recurrence.

The tumor macroenvironment (organism level) includes physical elements and infectious, drug, and other chemical agents to which people are exposed. It is influenced by behavioral, lifestyle, economic, and cultural factors such as diet, physical activity, tobacco use, and reproductive history and behaviors.

Because the influence of the macroenvironment on cancer is inherently complex, research to characterize that influence must be varied and multidisciplinary and include initiatives to handle the collection, storage, and analysis of complex data. NCI will:

- Foster the development of shared, investigator-accessible data systems that integrate patient and population data from multiple case-control and cohort studies. These systems will enable researchers to investigate the roles of macroenvironmental, genetic, and other personal susceptibility factors in modulating cancer risk.
- Support the statistical and methodologic research needed to assess and quantify macroenvironmental exposures such as dietary intake and physical activity and their impact on cancer risk, contribution to the cancer burden, development and evaluation of health policies, prevention and screening interventions, and communication of risk factors to the general public, health providers, and policy makers.
- Advance preclinical and clinical studies to improve our understanding of the biological and molecular basis of macroenvironmental exposures on cancer development or prevention. We will apply this knowledge to identify biomarkers of harmful exposures or early tissue damage that will improve early detection of cancer.
- Support integrated transdisciplinary research to determine the impact of various genetic, behavioral, and sociological factors on health behaviors, health policy development, and other influences on the equitable delivery of care and health-related societal trends.
- Foster dissemination of evidence-based approaches for reducing exposure to harmful macroenvironmental agents and promoting adoption of healthful behaviors to individuals, communities, and populations.

These investments will improve our understanding of the role of lifestyle and environment in carcinogenesis, identify the specific physiological mechanisms at work, and elucidate the interaction of the macroenvironment with personal susceptibility factors such as genetic background. This information will be critical in developing interventions for the prevention, early detection, diagnosis, and treatment of cancer patients and survivors.



STRATEGY 1.3—Increase our understanding of the behavioral, environmental, genetic, and epigenetic causes of cancer and their interactions.

A firm understanding of the underlying causes of cancer incidence, suffering, and mortality is fundamental to the development and delivery of effective public health and medical interventions. Reaching these insights will require large-scale consortial studies to assess the impact of potential behavioral, sociocultural, environmental, epigenetic, and genetic cancer risk factors and their interactions, products, and effects in human populations. NCI will support large-scale epidemiologic consortial studies that complement the work of independent investigators and provide sufficient statistical power and scientific expertise to rapidly generate and conclusively answer relevant questions. These transdisciplinary and translational studies will be capable of incorporating emerging models, technologies, and informatics strategies to obtain, organize, and integrate substantial amounts of highly complex data. We will:

- Facilitate the collaboration of clinical and epidemiologic researchers with one another and with scientists in molecular, genomic, and other high-throughput technologies to conduct cohort, case-control and family-based studies.
- Support the development of study designs, approaches, themes, and organizations to address differences in cancer occurrence and its consequences among all populations.
- Facilitate study design standardization to allow data compilation, analysis, and sharing across the research community.

- Develop the flexible mechanisms and infrastructure for providing scientific input, oversight, and support that will make these large-scale enterprises possible within a cost-effective framework.
- Foster the dissemination of the results of studies on the demographic, environmental, and genetic causes of cancer to provide the evidence base for public health and medical interventions.

The knowledge gained through these studies will be particularly useful in elucidating the underlying reasons for racial, ethnic, geographic, and international differences in risks, multigenerational factors, and the etiology of understudied malignancies.

Strategic Partnerships Advance Studies in Molecular Epidemiology

Powerful new tools generated by recent advances in genomics and the molecular sciences have provided an unparalleled opportunity for scientists to accelerate knowledge about the genetic and environmental components of cancer initiation and progression through studies in molecular epidemiology. Strategic partnerships link epidemiologists with one another and with genomicists and other investigators from the clinical, basic, and population sciences to complement the traditional research model based on individual investigators or independent groups. This approach is speeding the discovery of causal agents and pathways, early detection markers, and interventions designed to prevent and control cancer. Strategic partnerships can build the synergy to respond to a growing consensus in the scientific community that the full potential of genomic and other emerging technologies will require large-scale consortial studies. These studies have the efficiency and power to identify common low-penetrant susceptibility genes and related gene-gene and gene-environment interactions. One such partnership is the Consortium of Cohorts, an international collaboration of investigators responsible for 23 independently funded population cohorts involving 1.2 million individuals. Other consortia are investigating family-based data and less common cancers that cannot be easily evaluated in traditional studies.

STRATEGY 1.4 — Identify and characterize the influence of the microenvironment on the chain of events that leads to cancer initiation and progression.

The microenvironment plays a critical role in cancer initiation and progression and may be an important factor in prevention and treatment intervention development. NCI will develop initiatives to investigate the microenvironment of different tumor types, such as colon, brain, prostate, breast, and lung. We will:

The microenvironment (tissue level) is composed of stromal cells, the extracellular matrix, growth factors, and other proteins produced locally and systemically. It plays a critical role in tumor initiation and progression and can limit the access of treatment to the tumor, alter drug metabolism, contribute to the development of drug resistance, and otherwise influence clinical outcome.

- Support research to investigate stromal cells in the tumor microenvironment as potential targets for cancer prevention and treatment interventions. This research will clarify the precise nature of normal stromal cells and seek to understand how stromal cells are altered during tumor progression and reciprocally influence tumor initiation and progression.
- Advance studies to identify alterations in other components of the tumor microenvironment that are critical in development of the malignant phenotype.
- Support research to identify tumor stem cells and characterize the interactions between these cells and stromal cells.
- Continue investigations to describe the role of inflammatory and immune cells in tumor initiation and progression.
- Foster development of novel technologies and model systems for better understanding the tumor microenvironment and for developing tissue- or cell-specific targeting agents.

These investments will improve our understanding of the tumor microenvironment and permit the development of effective therapeutics associated with minimal drug resistance, diagnostic tests that assess the state of the microenvironment, and novel interventions for cancer prevention.

Integrative Cancer Biology Promises New Leads for Prevention, Detection, Diagnosis, and Treatment

An integrative approach to cancer research that combines multiple disciplines and taps the best available resources is essential. Studies in molecular epidemiology identify the multiple and complex causes of cancer. Integrative cancer biology elucidates the dynamic and spatial interactions among molecules in a cell, among cells, between cells and their microenvironment, and between the organism and its macroenvironment, and considers differences in patient response to disease and treatment caused by individual genetic variation. These interactions are potential targets for new and more rationally designed interventions to prevent, detect, diagnose, and treat cancer.

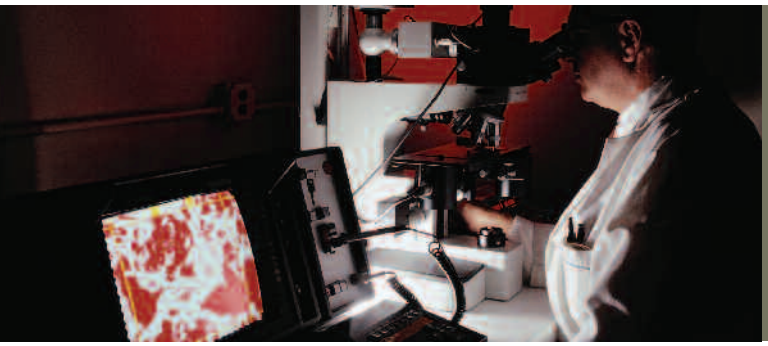
Scientists know that a cell becomes malignant as a result of changes to its genetic material and that accompanying biological characteristics of the cell and its surrounding microenvironment also change. Genetic mutations in an evolving cancer cell result in proteins that do not function correctly. These dysfunctional proteins disrupt the intricately balanced molecular communication networks of the cell. Using data derived from research on the tumor micro- and macroenvironments, scientists will create computational models of these complex networks to help develop new ways to preempt the development and progression of cancer. New NCI-supported Integrative Cancer Biology Programs have already begun the development of reliably predictive computational models of cancer initiation, promotion, and progression; the integration of experimental and computational approaches for understanding cancer biology; and the support of integrative cancer biology as a distinct field. In addition, researchers continue to develop animal models that mimic the development of cancer in humans and powerful tools for imaging molecular interactions, integrating large datasets, and validating computational models.

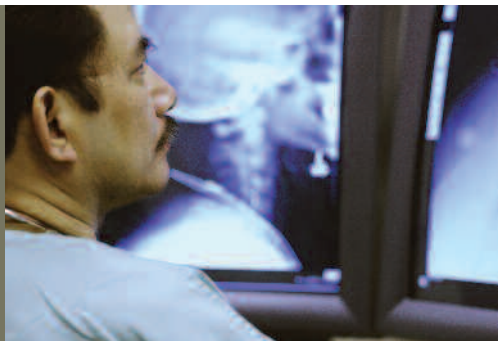
STRATEGY 1.5 — Use an integrative approach to gain a comprehensive understanding of the mechanisms of cancer initiation and progression and their implications for diagnosis and treatment.

Cancer remains one of the most complicated and difficult diseases to diagnose and manage. A systems approach is needed to both integrate information and data and meld the cultures and disciplines needed in this enterprise. NCI will support a broad set of interactions and efforts, both within NCI and across the scientific community, to develop an integrative approach to understanding cancer. We will:

- Build critical working connections among various disciplines including the traditional basic, clinical, and epidemiologic research communities and fields as disparate as computational science, physics, engineering, mathematics, and systems design.
- Support the generation, integration, and analysis of the vast amounts of biological information prerequisite to this research approach.
- Support development of analytic approaches that use nanotechnology and other advanced technologies to improve quantitative measurement of both traditional and new parameters, ranging from the single cell to the population level.
- Encourage application of integrative cancer biology to various programs within NCI to begin to unite and leverage this approach to cancer research.

Once this higher order systems understanding is achieved, it can be used in numerous ways in pursuit of rational treatment design. The full circle of investigation will involve synthetic biology to generate new approaches and agents based on cancer cell design principles.





Diverse Technologies Support Research into the Causes and Mechanisms of Cancer

Advanced technologies are pivotal in identifying the complexities of cancer susceptibility, initiation, and progression.

- Genetic and protein microarray analysis, nanotechnology, molecular imaging, and high throughput screening are helping scientists to identify many of the complex cellular mechanisms responsible for cancer.
- Tissue and animal models, laser capture microdissection, molecular profiling, molecular imaging, nanotechnology, and computational modeling are aiding our understanding of the interaction of cancer cells with the host microenvironment.
- Advanced genomic technologies, including population level genetic screening, whole genome scans, and high throughput screening are allowing us to identify genetic variations that make certain individuals more vulnerable to specific environmental carcinogens.
- Advanced statistical techniques assist scientists in analyzing the impact of the macroenvironment on cancer. Assays for biomarkers, for example, are used in research to assess the contribution of dietary factors and other environmental exposures on cancer risk.
- Nanotechnology-based probes used to image molecular pathways of cancer will allow detection of early disease and non-invasive monitoring of interventions. Other advances in nanotechnology will facilitate *in vivo* monitoring of individuals at risk for cancer and patients with disease.
- Bioinformatics platforms are central to applying the full potential of advanced technologies to invigorate cancer research.

STRATEGY 1.6 — Develop and utilize emerging technologies to expand our knowledge of the risk factors and biologic mechanisms of cancer.

It is critical that emerging technologies for enabling comprehensive molecular analysis of tumors are used effectively to gain a better understanding of the causes and mechanisms of cancer and to produce more effective interventions to preempt cancer before it becomes a life threatening disease. Applying technologies such as high-throughput genotyping, genomics, proteomics, molecular imaging, and nanotechnology in a standardized manner will be necessary to generate data that are consistent and comparable. NCI will:

> Facilitate development of standardized methodologies and robust, validated approaches for analyzing and reporting data.

> Support the development of standards for evaluating the performance of multiple technology platforms. This will include:

- Creating dedicated centers and consortia to facilitate a multidisciplinary team approach for applying these technologies to meet specific scientific needs with minimal infrastructure duplication.
- Supporting development of an informatics infrastructure for these centers to ensure that the data are analyzed consistently and are easily available to the cancer research community.
- Supporting cancer molecular profiling projects and ensuring rapid dissemination of the data generated.

> Emphasize development of data-related protocols and standards for dissemination to the broader research community.

> Apply the data generated from this research to inform molecular imaging and nanotechnology development.

By maximizing the use of emerging technologies, we will be able to develop interventions to identify individuals at risk for cancer, detect early-stage disease, and improve patient management.

Highly Lethal Cancers Are Still a Mystery

While we have made great strides in improving the odds for some cancers, others are still largely mysterious to scientists. In 2005, about 32,180 people in the United States will be diagnosed with pancreatic cancer. There will be about 14,520 new cases of esophageal cancer, and an expected 17,550 people will be told they have liver cancer. These are highly lethal diseases with poor five-year survival rates.

Epidemiologists have already identified several risk factors in common for these three cancers, including chronic inflammation, tobacco and alcohol use, and obesity. However, the relative rarity and high lethality of these cancers make it difficult to conduct the large population studies needed to draw valid statistical conclusions about the roles of genetic, environmental, and lifestyle factors in their initiation and progression. In contrast, it is not unusual for population studies of breast or prostate cancer to enroll tens of thousands of participants. NCI will work to address the challenge of relatively low numbers of patients with highly lethal cancers by developing a consortium of investigators to pool the resources of multiple institutions to conduct epidemiological studies of these groups. Through the collection, storage, management, and sharing of data for a large numbers of cases, investigators will be able to amass enough knowledge to evaluate the possible combinations of genetic, environmental, and lifestyle factors—from molecular to behavioral—that are causing these cancers.

STRATEGY 1.7 — Elucidate the relationship between cancer and other human diseases.

The success of early intervention in the cancer process will depend on developing a clearer appreciation and understanding of the interface between cancer and other diseases. For example, researchers have shown associations between cancer predisposition and hepatitis B virus, HIV, and other forms of immune dysfunction; chronic gastrointestinal inflammation; obesity; and diabetes. NCI will:

- Conduct epidemiologic studies to identify new associations between cancer and other diseases and provide a clearer delineation of those already identified, carry out mechanistic analyses to bring insight into these relationships, and develop innovative intervention strategies that will interfere with development of the associated cancers. These studies will be conducted in partnership with other NIH Institutes and the pharmaceutical industry and will leverage the expertise of investigators, researchers, and clinicians. This collaborative approach will expedite progress in identifying at-risk populations and developing new methods for detecting, treating, and preventing cancer and other chronic diseases.
- Utilize the molecular epidemiologic cohorts developed for cancer studies to identify the causal pathways for other diseases and vice versa.
- Carry out follow-up investigations when credible preliminary evidence suggests that a drug used for preventing or treating other diseases may also be effective in cancer prevention or treatment.

Effective interventions against one form of human disease, such as cancer, often synergistically influence their application against other diseases. Conversely, the prevention and early detection of other diseases may have clinical application and economic efficacy for cancer and other conditions.

STRATEGIC OBJECTIVE 2

Accelerate Progress in Cancer Prevention

We will accelerate the discovery, development, and delivery of cancer prevention interventions by investing in research focused on risk assessment, systems biology, behavior modifications, environmental and policy influences, medical and nutritional approaches, and training and education for research and health professionals.

Prevention is our first line of defense against cancer. Preventing cancer focuses on understanding and modifying behaviors that increase risk, mitigating the influence of genetic and environmental risk factors, and interrupting carcinogenesis through early medical intervention. Dramatic developments in technology and a more complete understanding of the causes and mechanisms of cancer will enable us to provide more effective ways to prevent the disease. Identifying critical molecular pathways of pre-cancers will provide new drug targets for preempting cancer. Transdisciplinary research will provide a more complete understanding of the interplay of molecular, behavioral, genetic, and other factors contributing to cancer susceptibility. We must systematically identify the most promising advances, harness their application for new prevention approaches, and encourage and monitor the adoption of prevention interventions in public health and clinical settings. It is imperative that evidence-based advances shown to inform and motivate people are disseminated and made accessible.

STRATEGY 2.1 — Develop a transdisciplinary systems approach to explore the biology behind successful cancer prevention.

Cancer is a complex array of diseases that are not always demonstrated or predicted by examining individual processes, thus making cancer prevention exceedingly challenging. NCI will use a systems biology approach, emphasizing early events and modifiability to develop effective cancer prevention strategies[1]. We will:

- Build teams to merge laboratory, epidemiologic, and clinical approaches for identifying factors that influence cancer initiation and progression and improve the effectiveness of preventive interventions.
- Support the development and use of technologies that incorporate and analyze detailed genomic, epigenomic, transcriptomic, proteomic, and metabolomic information to determine individual cancer susceptibility and detect precancerous conditions.
- Support the use of technologies to identify and validate molecular targets that can be modulated to reduce cancer occurrence and progression and to identify robust biomarkers that will inform patient-specific risk/benefit analyses for prevention regimens.
- Develop molecular imaging techniques to non-invasively detect modifications to molecular targets or biomarkers influenced by cancer prevention interventions.
- Use and develop model systems to accelerate progress in identifying individuals who are likely to respond to cancer prevention approaches.
- Support research to elucidate the mechanisms of tobacco addiction and control and encourage research to identify specific bioactive food components, dietary and physical activity patterns, and other lifestyle factors to further understand how they contribute to cancer prevention as well as to carcinogenesis.
- Integrate preclinical and clinical investigations that incorporate the newest approaches and technologies within the biological and psychosocial domains to speed discovery of early detection biomarkers and preventive agent development.

Building on the totality of information available about cancer processes, we will be able to expand the number of effective cancer prevention strategies and help identify target populations and individuals who will benefit most from specific interventions.

[1] See Objective 1 to learn more about NCI's research efforts aimed at further understanding the biological mechanisms underlying cancer susceptibility.

Diet Is an Integral Part of Both Cancer Prevention and Treatment

Prevention

Mounting evidence with animal models suggests that the use of foods and their components are an appropriate preemptive strategy to halt or reverse several steps in the cancer process. Likewise clinical studies point to several foods and their components as modifiers of cancer risk. Nevertheless, it is clear that not all individuals respond identically to the health benefits associated with specific foods or their components. Much of this variability in response likely reflects genetic differences among people, the amount of specific foods consumed, and the timing of intake. As we learn more about gene-nutrient interactions, we will have a clearer understanding as to who will benefit most from dietary interventions and what amounts of foods or supplements will be needed to maximize benefits while minimizing possible adverse effects.

Treatment

Cancer and cancer treatments can lead to food aversions and precipitate nutritional deficiencies. Nausea, vomiting, diarrhea, constipation, mouth sores, swallowing complications, and overall pain can not only influence eating behaviors and reduce the intake of energy and protein but also decrease the intake of a number of bioactive food components needed by patients. These deficiencies can, in turn, cause a patient to be weak, tired, and unable to resist infection. Studies are currently underway to identify sensitive biomarkers which can be used to evaluate the nutritional status of patients and determine what dietary shifts are needed to optimize chemo- or radiation therapy and promote healthy recovery.

STRATEGY 2.2—Develop and test behavioral approaches for reducing cancer risk, focusing on tobacco prevention and cessation, diet, exercise, weight management, sun safety, cancer screening, and avoiding excessive alcohol use.

More than half of all cancers are partially related to modifiable behavioral factors that affect the risk for cancer at all stages of its development. These include tobacco use, diet, physical inactivity and excess weight, sun exposure, cumulative exposure to radiation, failure to get cancer screening, and excessive alcohol use. Research is needed to understand and address these factors for patients across all age groups, racial and ethnic populations, socioeconomic strata, geographic areas, and with cancer diagnoses. NCI will:

The evidence is now clear that obesity is a significant risk factor in many cancers. Overweight and obesity in the United States may account for 14 percent of all cancer deaths in men and 20 percent in women, adding up to more than 94,000 deaths each year. In women, increased body mass is associated with higher rates of cancers of the breast, endometrium, cervix, and ovary. In men, excess weight increases stomach and prostate cancer risk.

- Support integrated, multidisciplinary studies of behavior and behavioral change, taking into account the social, psychosocial, environmental, lifestyle, policy, cultural, and biological and genetic determinants of cancer.
- Support research to understand how people perceive risk, make informed and shared decisions regarding behavior, and maintain healthy behavior or change risky behavior.
- Support research to develop innovative behavioral and community-based interventions to promote preventive and health maintenance behavior.

There are significant barriers to getting people to change their behaviors. A greater understanding and dissemination of research and best practices on how to motivate people to adopt healthy behaviors will help reduce cancer risk for individuals and communities and ultimately decrease cancer incidence.

STRATEGY 2.3—Study the impact of environmental and policy interventions on cancer risk.

Environmental and policy interventions focusing on efforts such as restricting tobacco sales to minors, increasing the price of cigarettes, and instituting smoke-free workplaces and public places have been found to reduce tobacco use. A supportive physical environment that provides features such as walking paths, sidewalks, bike paths, and attractive stairwells has been shown to encourage physical activity. NCI will:

- Support research on population-based behavior and how to change risk behavior and reduce cancer risk through environmental and other policy.
- Advance research to assess behavior change resulting from health campaigns that promote the availability of healthy foods in a variety of settings, such as fast food restaurants and schools, and changes to the built environment encouraging physical activity. Investigate how best to overcome barriers to screening and medical care such as lack of transportation and limited availability and implement policies that provide insurance coverage for prevention and early detection services. Investigate the impact of comprehensive clean indoor air laws on tobacco use behavior.
- Develop analytic strategies to evaluate interventions targeting the environment and lifestyle and the influence of behavioral, social, and psychological factors on those interventions.

Scientific evidence regarding the effectiveness of environmental and policy interventions will inform future decision making and lead to public policy that promotes the adoption of healthy behaviors and the prevention of many cancers.

Reducing Tobacco Use Is Still a Major Cancer Prevention Strategy

Lung cancer is the leading cancer killer in both men and women with annual rates in recent years of more than 163,000 deaths and over 172,000 new cases diagnosed. Researchers estimate that 87 percent of lung cancer cases are caused by smoking.

Cigarette smoke contains more than 4,000 different chemicals, many of which are proven cancer-causing substances, or carcinogens. The longer a person smokes, the greater his or her risk of lung cancer. When a person stops smoking, the risk of lung cancer begins to decrease. After ten years, the risk drops to one third to one half the level of people who continue to smoke. Many of the chemicals in tobacco smoke are also carcinogenic for people who inhale secondhand smoke, which is responsible for approximately 3,000 lung cancer deaths each year.

New medications to help smokers quit are under development and current evidence shows that information and referrals from quit phone lines as well as behavioral counseling from healthcare providers significantly increase the numbers of people who quit.

STRATEGY 2.4 — Develop medical interventions that suppress cancer initiation and progression.

Scientific advances are providing new evidence for the potential use of drugs, vitamins and minerals, vaccines, food constituents, and other substances to slow, halt, or reverse precancerous conditions in people at risk for cancer. NCI will:

- Support a robust cancer prevention agent development program to identify the most promising synthetic and natural agents to prevent or delay cancer onset.
- Advance studies to identify agents that interfere with carcinogenesis by affecting cellular targets.
- Support large-scale clinical trials to test the ability of these agents to modify biomarkers of carcinogenesis and ultimately to prevent or delay cancer onset.
- Continue to support a consortium of research centers for conducting clinical trials to assess the potential of new agents and other approaches to inhibit the cancer process.

Medical interventions, in combination with lifestyle and environmental changes, hold great promise to dramatically reduce cancer incidence in future generations.

STRATEGY 2.5—Develop and support a periodic systematic review of the epidemiologic evidence on possible carcinogens and other cancer risk factors.

With an ever increasing number of published epidemiologic studies exploring suspected carcinogens and other cancer risk factors, public health and clinical practitioners, regulatory agencies, and policy makers need authoritative and rigorous evidence-based reviews that integrate the knowledge gained from individual studies to identify meaningful findings. NCI will:

- Support the development of a guide to cancer risk factors, similar to the prevention research evidence reviews reflected in the *Guide to Community Preventive Services* and the *Guide to Clinical Preventive Services*.
- Continue to work through the Interagency Cancer Epidemiology Research Funders to identify funding partners, develop an administrative structure for this project, implement a peer-reviewed process for nominating and completing evidence-based reviews, and develop a dissemination plan to deliver valid evidence-based cancer prevention interventions to targeted audiences.
- Continue to work with the International Agency for Research on Cancer to develop monographs on the Evaluation of Carcinogenic Risks to Humans.

Reviews such as these will identify evidence on carcinogens and other social, behavioral, lifestyle, and environmental risk factors that is clear and consistent enough to justify public health policy and/or regulatory action[2].

[2] See Objective 5, Strategy 5.6, to learn about NCI's research on how to disseminate, adopt, and implement new cancer interventions.

STRATEGY 2.6 — Apply new knowledge and best practices to rapidly increase the adoption of evidence-based cancer prevention interventions in public health and clinical practice settings.

The most progress will be made in preventing cancer when new approaches to cancer prevention are widely disseminated, adopted, and implemented. NCI will support research and programs to increase the demand for and use of evidence-based cancer prevention interventions in public health and clinical practice and to influence cancer prevention policies.

STRATEGY 2.7 — Develop and sustain a prevention outcome monitoring system to evaluate the impact of dissemination and diffusion programs on the prevalence of evidence-based prevention interventions over time.

While cancer surveillance systems like the Surveillance, Epidemiology, and End Results program (SEER), when linked to clinical service payment systems like Medicare, can monitor the uptake of treatment innovations in defined populations of cancer patients, no comparable system exists for monitoring the adoption of evidence-based cancer prevention interventions in public health or clinical practice. We will examine existing NCI platforms that might help address this need and work with other agencies, including the Agency for Healthcare Research and Quality and the Centers for Disease Control and Prevention, to explore opportunities to collaborate and cooperate in initiating such a monitoring system. These efforts will set the stage for developing a new and unique system to track the diffusion of cancer prevention innovations and determine the association between changes in cancer risk factors and the success or failure in adopting evidence-based prevention interventions.

The Cancer Control PLANET World Wide Web portal brings together information about new evidence-based tools that can help public health officials assess the cancer and/or risk factor burden in a given geographic area, identify potential partner organizations, understand current research findings and recommendations, access and download information about evidence-based programs and products, and find guidelines for planning and evaluation. Go to cancercontrolplanet.cancer.gov.

STRATEGY 2.8 — Equip scientists, clinicians, and other health professionals with the principles, methods, and practices needed for cancer prevention research and education.

Strategies to prevent cancer depend on a cadre of investigators and practitioners. NCI will build a comprehensive education and training program in cancer prevention and control at the graduate and postdoctoral levels and for continuing education. We will prepare people to participate effectively in cancer prevention as a multidisciplinary process that incorporates the most recent advances and technologies in the genetic, molecular, behavioral, nutritional, and social sciences as well as those used in traditional health sciences such as epidemiology, environmental health, and biostatistics. We will use a comprehensive training initiative to encourage and support innovative transdisciplinary research and professional development. Additionally, NCI will build upon its efforts to bring the science and practice of cancer prevention to developing countries through fellowships and summer short course exchange programs.

The NCI Cancer Prevention Fellowship Program provides postdoctoral training opportunities in cancer prevention and control. The purpose of the program is to train individuals from transdisciplinary health sciences in the field of cancer prevention and control. For more information, go to cancer.gov/prevention/pob. For information on the full range of fellowships and internships supported by NCI, go to cancer.gov/researchandfunding/fellowships.

Large-Scale Clinical Trials Are Integral to Cancer Prevention Drug Development

Large-scale, chemoprevention trials are a final step in a long and careful research process to identify medicines, vitamins, minerals, or food supplements that help to prevent cancer. These multi-year trials monitor large numbers of healthy people who are assigned to take either the test chemoprevention agent or a placebo. Investigators analyze outcomes data to determine whether fewer people in the group taking the test agent develop cancer in comparison with the placebo group. Data on side effects are used to weigh the potential risks versus benefits of widespread and individual use of the prevention agent. Recent NCI-supported chemoprevention trials have led to the FDA approval of tamoxifen for breast cancer prevention and have demonstrated the feasibility of prostate cancer chemoprevention.

(Large-Scale Clinical Trials cont'd)

Trials for Breast Cancer Prevention

The Breast Cancer Prevention Trial (BCPT) was coordinated by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and enrolled over 13,000 women at more than 300 centers in the United States and Canada. This study led to the 1998 FDA approval of tamoxifen (Nolvadex®) for breast cancer prevention in women at high risk for the disease. Because of rare, but serious, side effects associated with tamoxifen use, NCI is supporting clinical trials of other breast cancer prevention drugs. The NSABP-coordinated Study of Tamoxifen and Raloxifene (STAR) is one of the largest breast cancer prevention studies ever. STAR is designed to compare the preventative effects of raloxifene (Evista®) and tamoxifen in postmenopausal women. The more than 500 participating centers across the United States, Puerto Rico, and Canada have completed enrollment of over 19,000 postmenopausal women at increased risk of breast cancer. STAR data may be released as early as 2006.

Trials for Prostate Cancer Prevention

The Prostate Cancer Prevention Trial (PCPT) was designed to test whether the drug finasteride (Proscar®) can prevent prostate cancer. This study, coordinated by the Southwest Oncology Group (SWOG), enrolled nearly 19,000 men at more than 200 centers in the United States and Canada. The trial was stopped early in June 2003 because of a clear finding that finasteride reduced the incidence of prostate cancer. However, men who did develop prostate cancer while taking finasteride experienced a slightly higher incidence of high-grade tumors. Researchers are continuing to analyze the data to find out whether finasteride actually caused these high-grade tumors.

The Selenium and Vitamin E Cancer Prevention Trial (SELECT), also coordinated by SWOG, is the largest-ever prostate cancer prevention trial. This trial was initiated based on previous findings that selenium and vitamin E, alone or in combination, may substantially reduce the risk of developing prostate cancer. In 2004, over 400 SELECT sites throughout the United States, Puerto Rico, and Canada completed the enrollment of about 35,500 men age 55 and older. African-American men aged 50 and over were eligible to enroll because prostate cancer strikes African-American men earlier and more often than white men. The study will continue collecting data through 2011.

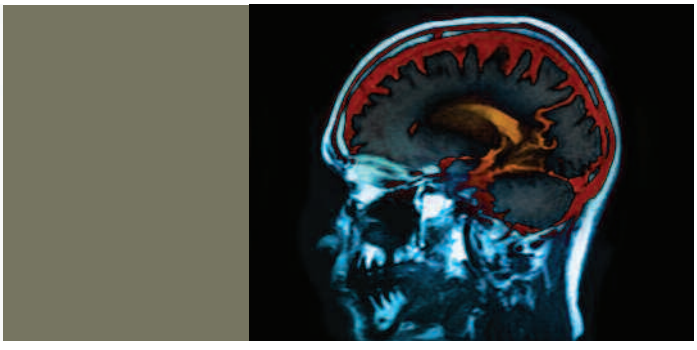
STRATEGIC OBJECTIVE 3

Improve Early Detection and Diagnosis

We will support the development and dissemination of interventions to detect and diagnose early-stage malignancy.

Detecting and diagnosing tumors early in the disease process, before the tumor becomes invasive and metastatic, can dramatically improve the patient's odds for successful treatment and survival and eliminate a large proportion of cancer deaths. For example, evidence suggests that 90 percent or more of colorectal cancer deaths could be prevented if precancerous polyps were detected with routine screening and removed at an early stage. However, the screening rate for colorectal cancer lags far behind that of other cancers, and the disease remains the second leading cause of cancer death in our Nation. For many other cancers—e.g., ovarian and pancreatic—there are no reliable early-stage screening tests to offer patients. For still others, such as lung cancer, screening tests are available but have not been proven to reduce mortality. Furthermore, although investigators continue to make promising discoveries that apply diverse technologies to early cancer detection, few of these advances have reached the patient.

By implementing the focused strategies described below, we will speed the translation of effective early detection and diagnostic approaches to the clinic. Healthcare providers and their patients will have access to sophisticated, minimally invasive procedures that harness imaging, proteomics, nanotechnology, and other advanced early detection and diagnostic techniques as well as improved access to and understanding of follow-up procedures.



STRATEGY 3.1 — Actively move research advances forward by bridging gaps across the translational spectrum.

Rapidly emerging discoveries in the laboratory promise better ways to distinguish cancer and early cancerous changes from normal tissue. To generate more effective markers for diagnosing cancer and predicting risk or treatment response, it is critical that we accelerate the movement of research findings into validation studies and clinical research where their true potential can be determined. We must improve the flow of information from basic research to development, validation, and clinical application and enhance information feedback from the clinic to basic research. NCI will:

- Support research to identify and validate specific molecular changes that occur progressively in cancer and that can be used as early diagnostic markers.
- Support an Institute-wide initiative to accelerate the clinical translation of imaging discoveries for early detection and diagnosis.
- Encourage the movement of new research areas such as micro-RNA expression and epigenetics/epigenomics to development and clinical translation.
- Develop and deploy team science mechanisms to address the variety of skills and amount of work required for post-discovery development.
- Ease the movement of research findings to clinical validation by enhancing the use of mouse models for preclinical interventions.
- Encourage research collaborations and provide incentives for developing evidence-based interventions.

Improving the flow of information among researchers and with healthcare providers will accelerate the identification of early changes that cause or promote cancer progression or metastasis and help identify risk or prognostic markers useful for developing more personalized and successful treatment regimens.

STRATEGY 3.2—Promote collaborative multidisciplinary research for validating biomarkers of early detection and screening.

In the interest of public health, it is important to ensure that biomarkers provide accurate, convincing evidence for diagnosis and conform to regulatory requirements. In the last several decades, only a few biomarkers—e.g., the Papanicolaou (Pap) test for cervical cancer, the prostate-specific antigen (PSA) test, the CA 15-3 test for breast cancer, and the CA 125 test for ovarian cancer—have found their way to clinical application for either screening or disease monitoring. This has been, in part, due to the limited rigor of studies required for clinical validation. NCI will:

- Promote collaborative, multidisciplinary research to validate biomarkers for early detection and diagnosis.
- Support research to determine whether a biomarker test predicts the true presence or absence of disease for all individuals.
- Promote research that tests the biomarker in an adequate spectrum of patients with and without cancer and accurately summarizes the sensitivity, specificity, and other performance characteristics of the test.
- Encourage public-private partnerships to provide researchers with access to necessary technologies and other resources.
- Create innovative funding mechanisms to attract multidisciplinary teams of leading scientists into this field of research.

Using rigorously evaluated biomarkers for detecting and diagnosing cancer early in the disease process will dramatically improve the survival rate for cancer patients.

STRATEGY 3.3—Develop risk factor profiles for identifying patients who are likely to benefit most from cancer screening.

General population screening for early cancer detection, although desirable in the long term, is logistically difficult, currently inefficient, and very expensive. To effectively use the promising diagnostic screening techniques that have been discovered, we must first develop risk profiles to identify the people who are likely to benefit the most from screening. NCI will:

- Develop and test techniques to screen people for risk factors using gene assessment and imaging technologies, clinical presentation, and data on lifestyle, family history, and environmental factors.

- Establish a comprehensive database of risk factors to help researchers and clinicians identify people at high risk for cancer.
- Develop and validate technologies for testing and monitoring high risk individuals for early-stage cancer and make these tests cost-effective and available to all who need them, using the principles established by NCI, the Food and Drug Administration, and the Centers for Disease Control and Prevention. These technologies will include bioinformatics-enhanced image analysis, proteomic profiling of blood and tissue, and identification of unique biomarkers or panels of biomarkers to "fingerprint" disease.
- Develop approaches for monitoring, in a secure and confidential manner, individuals identified as high risk for cancer to establish proof of concept for a personalized medicine approach.

Access to resources will allow researchers to develop ways to identify those patients who can benefit from targeted cancer screening procedures, accelerate their ability to personalize cancer diagnostic procedures, and increase the interest of industry in further developing and commercializing these techniques.

Biomarkers Prove Useful for Detection, Diagnosis, and Treatment

A biomarker is a substance found in the blood, other body fluids, or tissues at high enough levels to indicate the possible presence of disease. Examples of cancer biomarkers (also called tumor markers) include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). These markers are produced either by the tumor itself or by the body in response to the presence of cancer or certain benign (noncancerous) conditions.

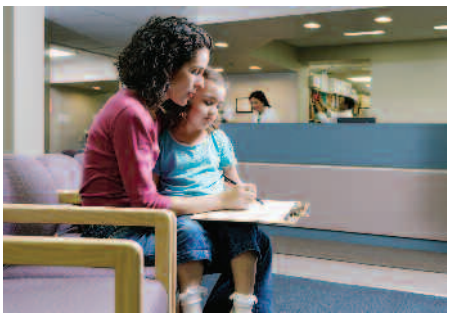
When used along with x-rays or other tests, measurements of tumor marker levels can be useful in the detection and diagnosis of some types of cancer. In addition, some tumor marker levels are measured before treatment to help doctors plan appropriate therapy. In some types of cancer, tumor marker levels reflect the extent (stage) of the disease and can be useful in predicting how well the patient will respond to treatment. Tumor marker levels may also be measured during treatment to monitor a patient's response to treatment. Finally, measurements of tumor marker levels may be a part of treatment follow-up to check for recurrence.

STRATEGY 3.4 — Encourage and provide investigator training to facilitate the development and application of diagnostic tests.

NCI must support training opportunities that will lead to collaborations among basic bench scientists, clinicians, population scientists, medical educators, and experts from other disciplines such as imaging and informatics. NCI will:

- Sustain training activities that encourage exploratory and developmental research, promote collaborations that bring together ideas and approaches from diverse scientific disciplines, and support businesses in conducting innovative research.
- Support training related to technology development, including high risk, early-stage research, and increase support for developing and validating technologies for early detection and diagnosis.
- Place greater training emphasis on innovative research activities that have high translation impact and go beyond strictly mechanistic studies.

Researchers from diverse fields who are prepared to collaborate will be better able to tackle questions about early-stage cancer diagnosis and establish a fertile environment for exchanging ideas and ensuring that only those diagnostic tests and applications with high clinical value are pursued.



STRATEGY 3.5 — Determine why abnormal findings from screening examinations have less than acceptable rates of follow-up and develop strategies to improve the system.

Research is needed to delineate the interventions necessary to ensure that health system and provider barriers are eliminated and that patients fully comprehend and recognize the importance of follow-up recommendations. New approaches are needed to link patients, providers, and advocates with health system information to ensure that patients receive and adhere to appropriate follow-up recommendations. To address these issues, NCI will:

- Collaborate internally and with other agencies to improve the level of participation of at-risk populations in screening programs, promote timely resolution of abnormal findings, and ensure uniform patient access to state-of-the-art treatments.

- Support public-private partnerships to develop needed information systems, support existing networks that have the capacity to conduct research in this area, and support workshops to develop consensus on measures for intervention and surveillance.
- Provide policymakers with the information they need to construct health policies that improve access and reduce barriers in the healthcare system.

The widespread use of existing screening tests in diverse public health settings accompanied by appropriate post-screening follow-up will significantly reduce cancer morbidity, mortality, psychosocial sequelae, and associated human and financial costs.

STRATEGY 3.6 — Develop better diagnostic and screening tools for early detection, risk assessment, and recurrence.

Increasing accuracy in the characterization of cancers at the time of diagnosis will allow physicians to develop the most appropriate treatment plan for individual patients. NCI will:

- Support the development and evaluation of high-throughput, cost-effective technologies that permit rapid and accurate patient diagnoses.
- Collaborate with patient advocacy organizations and groups conducting clinical trials to facilitate the secure and confidential collection of large numbers of tumor samples and other biospecimens. Associated clinical data on diagnosis and clinical outcome will be required for definitive evaluation of new diagnostic and screening technologies.
- Strengthen the development process with the expertise of interdisciplinary teams, including clinicians, pathologists, laboratory researchers, and statisticians.
- Conduct innovative clinical trials to test these technologies in diverse patient populations.

Validated screening and diagnostic technologies will allow clinicians to make earlier, more accurate diagnoses; identify the best therapies and preventive interventions for patients; and determine the likelihood that a tumor will recur.

STRATEGY 3.7— Make experimental data accessible across the cancer research community.

To be of maximum value to the cancer research community, experimental data must be accessible to all authorized researchers through intelligent broad-use software that offers interpretive and query functions. For example, research partners may require the exchange of data on genomics and proteomics. This level of shared data access will require user-enforced analysis and format standards so the data can be used for correlative studies. NCI will:

- Support the development of standards for submitting data into shared repositories and for inter-repository exchange. These standards will specify the minimum information required to correctly interpret experimental data housed in the repositories.
- Address the complex questions related to the feasibility of sharing raw data, including varying levels of user expertise and the intended use of the data. For example, raw mass spectra files from a proteomics experiment may be useful to developers of bioinformatics tools, whereas completed analyses of protein identifications with correlative data may be more valuable than raw data to biologists.
- Develop centralized or distributed registries to manage the electronic credentials needed to access data with security, privacy, or intellectual property limitations.
- Develop and apply guidelines to ensure that comparable data from various sources can be aggregated and that heterogeneous but related data sets—e.g., proteomics analyses and clinical assessments—can be integrated.
- Develop well documented programming interfaces that will allow researchers to mine large quantities of data.

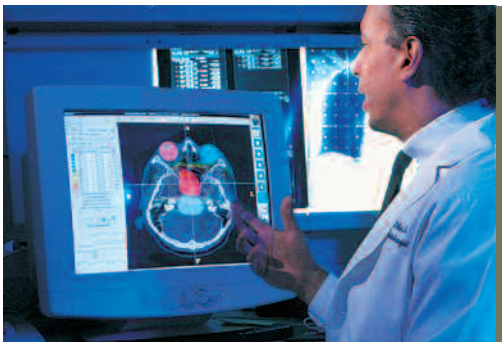
Improving shared research data access among multiple institutions and diverse groups of investigators will expedite the translation of research results into knowledge, products, and procedures to improve human health.

STRATEGY 3.8 — Translate evidence-based research into public health and medical practice.

We have made great progress in our ability to detect and diagnose early-stage malignancy. The challenge is to effectively disseminate best practices and evidence-based cancer screening approaches across all populations. Better understanding of risk perception and communication with patients and providers is key to successful adoption of research findings into practice. NCI will:

- Support programs to communicate the benefits, risks, and limitations of cancer screening tests, as well as screening alternatives, so that people can make informed decisions about obtaining cancer screening.
- Support research to proactively identify barriers to dissemination and to develop effective strategies for implementing and sustaining evidence-based screening.
- Forge linkages among scientists, communities, and the healthcare system responsible for cancer screening.
- Partner with other agencies and cancer advocates to develop innovative research dissemination programs that will close the gap between research findings and public health practice.

Effective delivery of information on cancer screening programs will facilitate early detection, make earlier intervention possible, improve patient odds for positive outcomes, and enhance quality of life.

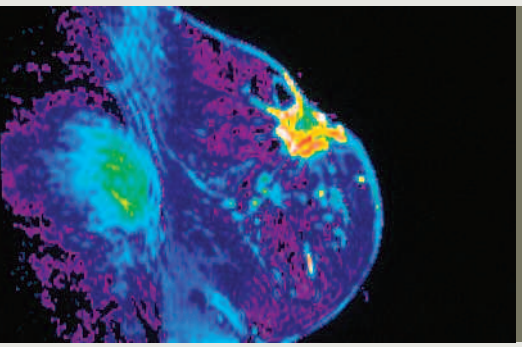


Understanding the Molecular Mechanisms of Metastasis Is a Critical Step in the Development of Better Treatments

Most cancer deaths are caused not by primary tumors, but by metastatic disease that is resistant to treatment. Yet, the biological mechanisms underlying metastasis are not completely understood. Researchers agree that tumor metastasis occurs in a series of steps. According to the prevailing hypotheses, the first step occurs when some cancer cells from the primary tumor become less adhesive to the cells around them, break loose, and enter either the circulatory or lymphatic system. Cells in the lymphatic system may come to rest in lymph nodes or may be carried into the blood stream. Cancer cells travel through the circulatory system to become lodged in capillaries, the microscopic blood vessels that supply tissues with oxygen and nutrients. Most cancer cells are larger than the diameter of the capillaries and become lodged in the first organ they encounter. A few continue on and come to rest at more distant sites. While most cancer cells die by this point, some survive to form metastatic tumors. Others lie dormant, sometimes for decades.

It has long been suspected and is now known that the interaction of an invading cancer cell and its microenvironment is instrumental in determining whether or not a new tumor will develop. Within the last decade, cancer researchers supported by NCI and others have learned much about the mechanisms involved in each step of the metastatic process. For example:

> Genetic signatures in some early-stage primary tumors appear to predict whether the cancer will eventually metastasize. This research may lead to prognostic tests to help physicians determine which patients will benefit from aggressive treatment options.



- New assay systems can detect individual detached cancer cells in a blood or tissue sample containing millions of normal cells. Researchers are using these assays to predict metastasis development, pinpoint the stage at which cancer cells begin to break free of the primary tumor, and identify genetic characteristics associated with survival and growth of metastatic cells.
- Cancer cells which overexpress the epidermal growth factor receptor protein grow best in tissues with high levels of specific proteins that activate this receptor. Furthermore, the levels of cytokines and other proteins that influence cell-to-cell interactions can alter the effectiveness of chemotherapy in metastatic tumors.
- When in the microenvironment of the bone, breast cancer cells produce more of a peptide[1] called PTHrP that causes resorption of bone. This resorption triggers the bone tissue to release proteins that stimulate new bone growth. However, these proteins also stimulate growth of the metastatic cells, which then produce even more PTHrP. In other words, a cycle is established where the natural response of the bone microenvironment to injury perpetuates the growth of the injurious cancer.

NCI will continue to place a high priority on research to understand the molecular mechanisms of cancer metastasis. The knowledge gained through this research will provide a tremendous resource to guide the development of interventions for cancer prognosis and treatment.

[1] A peptide is a protein fragment.

STRATEGIC OBJECTIVE 4

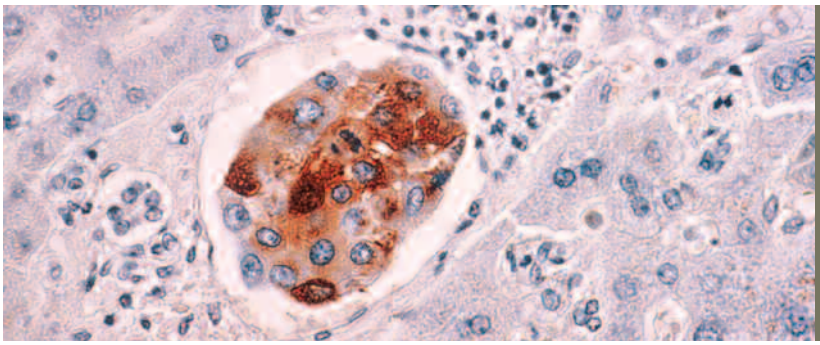
Develop Effective and Efficient Treatments

We will support the development and dissemination of interventions to treat malignancy by either destroying all cancer cells or modulating and controlling metastasis, both with minimal harm to healthy tissue.

Developing more efficient and effective cancer treatments that leave surrounding healthy tissue unharmed is at the heart of NCI's research agenda. These efforts build on our accelerated progress in preventing cancer and complement our increasing ability to thwart the progression of cancer to a metastatic state. Individualized therapies tailored to the specific characteristics of a patient's cancer provide hope that some cancers can be cured and many others managed as chronic diseases with little or no adverse effect on the daily lives or life expectancy of patients.

A strong understanding of the fundamental mechanisms leading to cancer progression and metastasis will dramatically improve our ability to identify key biochemical events in the disease process as targets for treatment. Accelerating target validation and the development of new treatment modalities will be possible through recent advances in biomedical technologies such as genomics, proteomics, metabolomics, nanotechnology, and imaging. Rapid translation from development to delivery will ensure that promising therapeutics move safely and efficiently from preclinical development through late-stage clinical trials and into clinical practice.

As with prevention and early detection research, we must anticipate scientific and technological advancements and enhance clinical research with interdisciplinary collaborations and a focus on translation into clinical practice. We must promote new and ongoing communication networks among researchers, oncologists, industry, and patient advocates and provide clinical trial investigators with a common clinical trials informatics platform. A highly interactive and optimally coordinated cancer clinical trials system will facilitate the effective conduct of small Phase I clinical trials for safety and efficacy, improve prioritization and coordination of large Phase II and III trials that test the efficacy of treatment for specific types of cancer, and remove barriers to the testing and use of combinations of treatment modalities.



STRATEGY 4.1 — Identify the molecular and cellular determinants of metastatic behavior.

Despite improved outcomes for many cancer types, patients with disseminated or metastatic cancer continue to have the poorest survival rates for all cancers. To change this reality, cancer researchers must gain new insights into the fundamental differences between metastatic and non-metastatic cancer. Recent advances in genetic profiling of tumors has led to the identification of several "metastatic expression profiles" present in the primary tumor, suggesting the existence of inherent genetic distinctions that can be used to identify tumors capable of metastatic behavior. Better animal models for studying metastatic behavior have also been developed. NCI will:

- Build on these advances by developing animal models for identifying relevant targets for treating metastatic cancers.
- Develop an easily accessible database of genes and signaling pathways that have been identified in multiple cancer models and species and validated as participants in the metastatic process.
- Support research to gain a better understanding of tumor stem cells and their role in human cancer at the molecular and functional level.

This coordinated investment will help expedite new insights into fundamental processes driving metastasis and enable identification of novel therapeutic targets and agents to preempt or control metastatic tumors.

STRATEGY 4.2—Validate cancer biomarkers for cancer prognosis, metastasis, treatment response, and cancer progression.

For most cancers, successful prevention depends on accurate risk assessment and successful treatment depends on early detection. Pioneering proteomic and biomarker advances and the promise of nanotechnology give us new hope for improved monitoring of cancer progression, metastasis, and treatment response. Improved biomarkers are crucial in ensuring that patients receive the treatments most likely to be successful in providing the best possible opportunity for survival. NCI will:

- Identify the proteins associated with cancers and employ recent advances in molecularly targeted imaging to locate very small tumors and interrogate their molecular features to assess prognosis.
- Refine and utilize high-throughput validation techniques to identify biomarkers for cancer prognosis, progression, metastasis, and treatment response.
- Create a library of validated biomarkers and make it available to the cancer research community.

STRATEGY 4.3—Accelerate identification, development, and validation of potential targets and strategies for cancer treatment by integrating preclinical and clinical research.

NCI will provide the leadership to turn molecular biology discoveries into valid, credentialed targets and to move the most promising preclinical leads to clinical testing. We will invest in effective infrastructures to promote a high degree of integration, coordination, and

communication along the discovery-development-delivery research continuum. Participants in all phases of research will need access to state-of-the-art enabling technologies. NCI will:

- Strengthen regional infrastructure to integrate preclinical science and early clinical testing. For example, NCI will facilitate the collaboration of clinical scientists, cancer modelers, and imaging researchers to develop novel imaging techniques for the preclinical assessment of specific targeted treatment agents that will enter clinical trials.

- Support cancer modeling and translational research to devise new preclinical tactics to identify biomarkers for assessing the efficacy, mechanism of action, and toxicity of promising treatment agents.
- Support preclinical researchers in the development of new imaging agents and approaches to overcoming important challenges to clinical research.
- Leverage NCI resources to establish public-private partnerships to expedite the selection of agents for movement into clinical testing.
- Augment the existing clinical trials bioinformatics infrastructure to give preclinical and clinical researchers easy access to the basic science knowledge they need for their studies.
- Link preclinical research data with a comprehensive database of clinical trial results to coordinate and optimize information and data sharing.

This integration and support for the preclinical and clinical testing of cancer interventions will accelerate selection and development of candidate treatment agents that are highly effective, less costly, and most likely to benefit patients.

New Nanotechnology Characterization Laboratory Supports Cancer Research and Development

NCI is engaged in an unprecedented effort to leverage the resources of government, industry, and academia in harnessing the power of nanotechnology to radically change the way we diagnose, treat, and prevent cancer. One initiative involves working in concert with the National Institute of Standards and Technology and the U. S. Food and Drug Administration to establish the Nanotechnology Characterization Laboratory (NCL). Scientists at the NCL perform preclinical efficacy and toxicity testing of nanoparticles and serve as a national resource and knowledge base to facilitate the regulatory review of nanotechnologies intended for cancer therapies and diagnostics. By providing the critical infrastructure and characterization services to nanomaterial providers, the NCL will accelerate the transition of basic nanoscale particles and devices for the development of new diagnostics, therapeutics, and preventives.

STRATEGY 4.4 — Develop a balanced approach for managing the toxicities of cancer therapy.

Minimizing the toxic effects of cancer treatment is critical to reducing morbidity and mortality. NCI will focus on developing molecularly targeted drugs that have fewer of the nonspecific, cytotoxic side effects that are commonly associated with traditional chemotherapeutic agents. We will:

- Support the concurrent development of tumor profiling devices such as gene or protein microchip arrays to inform the patient-specific selection of targeted therapies that will maximize patient response and minimize unwanted side effects.
- Foster the development of mechanisms for low-dose, site-specific drug delivery, such as aerosols that deliver agents to the lung and antibodies that selectively target drugs to cancer cells.
- Support the development of systems cell biology and computational modeling approaches to identify multiple cellular pathways that contribute to carcinogenesis and metastasis and that can be treated with low-dose, well-tolerated targeted drug combinations that uniquely affect cancer cells and spare normal cells.
- Invest in research to address the unwanted side effects caused by many useful, single-agent targeted therapies.
- Work with other NIH Institutes and Centers to better understand normal tissue toxicity and to identify and address gaps in research relevant to cancer treatment toxicity.
- Leverage initiatives under development at other Federal agencies that focus on toxicity assessments using nanotechnology, proteomics, genomics, metabolomics, and other advanced technologies.
- Support the application of these toxicology prediction techniques to minimize chemotherapy-induced collateral toxicity to organs not affected with cancer.

Minimizing toxicities will make it possible for more patients to complete therapeutic regimens and maximize the benefits of treatment.

STRATEGY 4.5—Integrate clinical trial structures to ensure expedited identification of the most promising treatment opportunities, rapid execution of the necessary clinical trials, and effective utilization of information and resources by clinicians.

Researchers have made substantial progress in developing new, more effective cancer therapeutics over the past thirty years. The timely development of even more sophisticated treatment approaches based on the molecular characteristics of a patient's tumor will require a restructured clinical trial enterprise. NCI will:

- Build new partnerships and multidisciplinary collaborations to ensure the unprecedented level of integration required to realize the tremendous potential for improved cancer treatments arising from current scientific advances.
- Coordinate and optimize patient-information and other data sharing by creating a comprehensive database of clinical trials and results.
- Create an integrated infrastructure to accelerate high-priority clinical trials implementation and eliminate redundancy.
- Develop patient recruitment strategies to ensure sufficient levels of participation from targeted populations.
- Collaborate with industry and healthcare providers to ensure that cancer patients have access to the best treatment available.
- Build on advanced technologies to assess the effects of drugs on molecular targets and pathways. Incorporate relevant biology studies into clinical trials to maximize our understanding of drug mechanisms and target effects in the context of human treatment.
- Create new partnerships and collaborations to accelerate the creation, development, validation, and utilization of these critical assays and tools.
- Rapidly deploy these resources in clinical trials of new agents and apply the knowledge gained to develop subsequent agents.

Greater integration of clinical trial components will accelerate the movement of effective interventions through clinical testing and set the stage for moving these interventions into public health and clinical practice.

"Omic" Technologies Support the Promise of Personalized Medicine

The sequencing of the human genome was the entry point into the scientific era of "omic" technologies, which now include genomics, proteomics, transcriptomics, and metabolomics. Omic science differs in its scope from earlier paradigms of research. While genetic studies for example, may seek to determine the role and function of individual genes, genomics is the study of the complete set of genes in the cell. Likewise, proteomics is the study of all cellular proteins and their impact on the cell's functioning. Transcriptomics focuses on the complete set of RNA transcripts present in the cell. RNA transcripts are an intermediate product in the cellular process of building proteins based on the DNA code. Metabolomics is the study of the complete set of cellular metabolites. The underlying principle of these omic technologies in cancer research is that the patterns of genes, proteins, RNA transcripts, and metabolites reveal important information about the status of the cell. Omic research applies comprehensive analysis technologies to detect the presence or activity of sometimes tens of thousands of these molecules at once.

Omic technologies provide the basis for much of the optimism surrounding the development of personalized medicine. Already, genomic and proteomic approaches for guiding treatment choices and monitoring response to therapy are under development. For example, NCI researchers recently used gene expression array, a genomic technology that scans the activity of thousands of genes from a tumor sample, to identify a genetic signature to distinguish aggressive from slower growing follicular lymphomas. This technique may provide a tool to guide patient-specific treatment choices, from watchful waiting to new treatments in clinical trials. Other NCI investigators are using proteomic technology to monitor the response of key pathways during therapy with several FDA approved molecularly targeted drugs to help assess whether the treatment is working. Omic technologies are also invaluable to the development of new targeted therapies for cancer. As omic research provides insight into the effect of cancer on the molecular workings of a cell, scientists can more readily identify molecular targets for drug intervention. Knowledge gained from omic technologies will also empower the development of other advanced technologies, such as *in vivo* nanotechnologies and molecular imaging, for targeted therapy. NCI anticipates that these and other omic-based advances in cancer research and care will help to hasten a new era of personalized medicine.

To ensure the best outcomes for all, we will work to:

5. Understand the Factors that Influence Cancer Outcomes

6. Improve the Quality of Cancer Care

7. Improve the Quality of Life for Cancer Patients, Survivors, and Their Families

8. Overcome Cancer Health Disparities

The successful application of evidence-based interventions for preempting cancer through prevention, detection, diagnosis, and treatment depends on our ability to quickly move effective interventions into practice. We must work to ensure that the results of our research and development efforts are adopted, that they accomplish their intended purpose, and that they adequately address issues in quality of cancer care, survivorship, and health disparities.

We will support and conduct research to better understand factors that influence outcomes by improving outcome measurement, expanding access to data, investigating behavioral and sociocultural influences on cancer outcomes and access to care, and better understanding how to disseminate the results of research and promote their use in public health, medical practice, and policy making. This understanding will inform continued efforts to improve the quality of care across the cancer continuum, improve the quality of life for cancer survivors and their families, and overcome cancer health disparities.

To Ensure the Best Outcomes for All

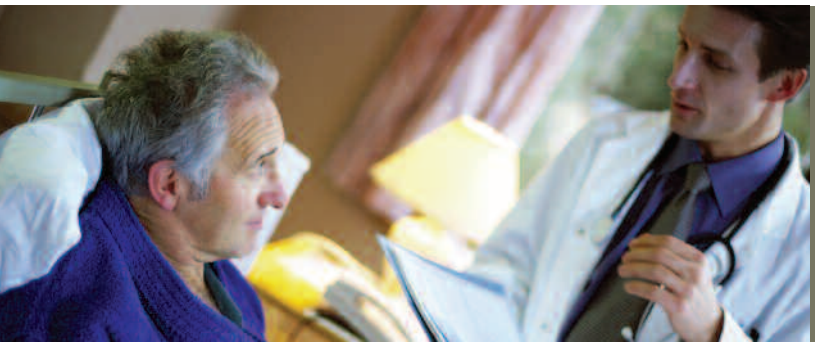
STRATEGIC OBJECTIVE 5

Understand the Factors that Influence Cancer Outcomes

We will support and conduct studies to increase our understanding of and ability to measure the environmental, behavioral, sociocultural, and economic influences that affect the quality of cancer care, survivorship, and health disparities.

It is critically important to advance a comprehensive, interdisciplinary research agenda to promote high standards of care, support reduction of the adverse effects of cancer diagnosis and treatment, and improve outcomes for all patients. Outcomes research describes, interprets, and predicts the impact of various influences on "final" endpoints that matter to decision makers, including patients, providers, private payers, government agencies, accrediting organizations, and society at large. These influences affect the extent to which public health programs and healthcare providers adopt recommended interventions, how successful the interventions are in addressing public health concerns, and how well patients adhere to provider recommendations. Outcomes may be measured in terms of survival, health-related quality of life, satisfaction with care, the performance of the health care system, and the economic burden on individuals or society.

NCI will support and conduct research to improve outcome measurement, expand access to data, and understand the influences on cancer outcomes and access to care. We also need to understand the barriers to dissemination and adoption of proven interventions in prevention, detection, diagnosis, and treatment. We must determine the best approaches to increase the use of evidence-based cancer interventions in public health and clinical practice and how best to use knowledge gained from research results to influence cancer policies.



STRATEGY 5.1 — Develop standardized measures of cancer care outcomes across the cancer continuum.

Research to identify and standardize measures is needed to support the creation, evaluation, and implementation of novel interventions to improve cancer outcomes. Toward this end, we will:

Final endpoints, such as survival, health-related quality of life, and societal economic burden, are distinguished from intermediate endpoints, such as rate of detection of early stage breast cancer, or clinical endpoints, such as degree of tumor shrinkage. Intermediate and clinical endpoints are critically important to the evaluation of an intervention.

- Support the development of surrogate endpoint biomarkers that detect events in molecular pathways integral to cancer prevention and early detection—e.g., biomarkers for accurate and efficient assessment of patient risk and drug efficacy in prevention clinical trials.
- Support research that identifies unwanted variations in patterns of care and enables us to better target quality improvement initiatives across the cancer care continuum.
- Develop psychometrically valid measures to characterize patient-practitioner interactions and thereby assess and improve these relationships.
- Develop informatics-based measures that allow clinical trials researchers and healthcare providers to monitor, recognize, and respond to patients' needs related to their functioning, symptoms and side effects, and health-related quality of life.
- Develop new partnerships with Cancer Centers, professional societies, and research consortia to support the development, testing, and implementation of evidence-based outcome measures.
- Identify measures specific to health disparities in cancer care and evaluate the effectiveness of screening, prevention, and treatment interventions intended to reduce those disparities.

STRATEGY 5.2—Identify research databases to study influences on cancer care and outcomes.

Epidemiologic surveillance helps investigators identify and characterize types, determinants, and outcomes of cancer and its treatment among various population groups. The combined use of cancer surveillance databases and electronic health records will deepen our understanding about what contributes to high quality cancer care from both biomedical and patient reported perspectives, taking into account ethnicity, socioeconomic status, and other demographic characteristics. NCI will:

The NCI National Clinical Trials Program provides an avenue for deepening our understanding of what contributes to high quality cancer care from both biomedical and patient reported perspectives. By incorporating health-related quality of life endpoints into clinical study design, we can assess the effectiveness of specific treatments and their influence on the quality of life for patients and survivors.

> Develop partnerships to link key data sources that track information on prevention and treatment interventions with NCI's surveillance programs to provide better insights into patterns of care and patient outcomes in the general population.

> Support development of tools for clinical modeling, evaluation, and cost-effectiveness and cost-benefit analyses of interventions that will ultimately assist care providers in advising patients about their care options.

> Support collection and analysis of detailed patient reported data to identify determinants of health care quality, trends, and the ability of delivery systems to foster positive outcomes related to quality of life, including body image, sexuality, fertility, and any physiologic late effects including second cancers.

Patterns of Care Tell a Story of the Patient Experience

The most favorable outcomes for cancer patients can be achieved only when cancer treatments of proven efficacy are effectively delivered in the general community. NCI draws from the Surveillance, Epidemiology, and End Results (SEER) registry data to investigate the adoption of recommended treatments for the most common cancers. Studies linking SEER and Medicare data continue to provide insights in the quality of care across all populations.

In addition, NCI has established large national-level studies that track patterns of care and outcomes for cohorts of newly diagnosed cancer patients. The first of these, the Prostate Cancer Outcomes Study provided a wealth of information about treatment outcomes for 3,500 men diagnosed with tumors confined to the prostate gland. Another large study, the Breast Cancer Surveillance Consortium investigates factors associated with high-quality screening mammography in community practice. Evidence from a study involving over 300,000 women, including 2,200 women with cancer, examined the combined and individual effects of breast density, age, and hormone replacement therapy on the accuracy of screening mammography. The results of these patterns-of-care studies are reported at professional meetings of oncology societies and are used to develop educational and training opportunities to improve the use of state-of-the-art cancer therapy in community practice.

STRATEGY 5.3—Increase the understanding of behavioral and sociocultural factors that influence cancer outcomes.

Integrating social, psychological, and communications research with biological research significantly improves our understanding of these factors and their relationship to disease prevention, quality of cancer care, and health outcomes. NCI will:

- Develop population-based data sets and complementary quantitative and qualitative research studies to better understand the relationships between behavioral risk factors and their impact on cancer incidence, prevention, quality of cancer care, survivorship, and health disparities.
- Promote strategic partnerships to study factors that influence health outcomes by examining traditional evidence-based systems and approaches as well as alternative and complementary medicine components of the cancer care delivery system. For example, we will support

interdisciplinary research on the adverse effects of cancer treatments, including identifying markers of susceptibility to these effects and gene-environment interactions.

- Conduct and support research on how social and psychological factors affect health communications and patient-provider decision making, and how race, ethnicity, literacy, and socioeconomic status influence these interactions.
- Collaborate with others to synthesize research with respect to the role of sociocultural, behavioral, emotional, and spiritual factors that affect patients' treatment and follow-up and health maintenance behaviors following treatment.
- Establish partnerships for and support community-based and health care delivery research to translate findings into policy to improve the quality of care and reduce cancer health disparities.

The Interface of Biological and Behavioral Sciences

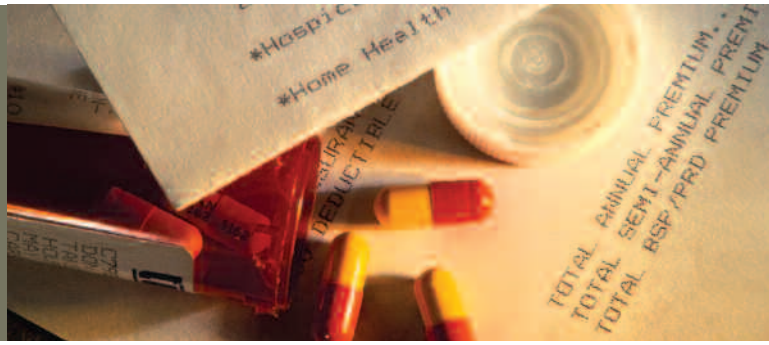
NCI supports and evaluates a comprehensive program of research to increase the quality of cancer prevention and control through the behavioral sciences. This includes the integration of genetic, epidemiological, behavioral, social, applied, and surveillance cancer research. This research is aimed at identifying the theoretical underpinnings of cancer-related behavior and behavior change across all ages, racial and ethnic groups, socioeconomic strata, and cancer diagnoses. For example, NCI supports research on cognition, emotion, stress, and pathways to health outcomes; links between education and health; social and cultural determinants of health; and mind-body interactions and health.

New interventions must be firmly grounded on scientific evidence, especially the findings that result from epidemiological and surveillance research. Epidemiological research is essential to assess the weight of evidence for particular cancer risk-reducing behavioral recommendations. Surveillance research and its application tells us where we are in our progress against cancer, generates hypotheses for more basic research and interventions, and provides important data for understanding the role of health services and policies on cancer outcomes. Research in epidemiology, cancer-related behaviors, and surveillance should be woven together inextricably to optimize progress in the control of cancer.

STRATEGY 5.4 — Increase our understanding of the factors that affect access to cancer care.

Disease always occurs within the social context of human circumstances, including social position, economic status, culture, and environment. To understand cancer incidence and outcomes, we need to understand the context in which they occur. NCI will:

- Partner with other Federal agencies, universities, the private sector, and local communities to support transdisciplinary research to identify barriers that prevent many people from receiving the best quality care and obtaining the best outcomes. This research will address systemic barriers such as fragmentation of care; financial barriers, including lack of health insurance or underinsurance; physical barriers such as distance to treatment facilities; knowledge, language, and education barriers for both patients and providers; and issues of culture and bias, both personal and institutional.
- Investigate factors that hinder people from participating in clinical trials of cutting-edge, state-of the-science treatments.



> Support participation in clinical trials through patient outreach, recruitment, and retention, especially in underserved populations.

> Investigate the economics of access to care by studying the comparative costs of reducing delays in patient diagnosis and receipt of follow-up care after abnormal findings, the comparative costs of treating specific cancers at an earlier rather than later stage of disease, and the cost-benefits of reducing cancer morbidity, mortality, and health disparities.

STRATEGY 5.5—Build sustainable community-based structures to support research on cancer outcomes.

Knowledge about what constitutes quality cancer care, how well it is being delivered, and what needs to be done to overcome inequalities and associated disparate outcomes resides within the communities where services are provided. NCI will:

> Support community-based research to include the perspectives of the patient or consumer and that of the healthcare provider to expand our understanding of cancer care generally and health disparities in particular.

> Support community-based research partnerships that generate better informed hypotheses, develop more effective interventions, and enhance the translation of research results into practice.

STRATEGY 5.6—Expand our understanding of how to disseminate research results and promote the adoption of evidence-based cancer interventions by a diverse population of patients, providers, and the public.

As new investments in basic and translational research close the gap between discovery and development, equally important is the need to close the gap between development and delivery. Doing so will require research to develop more effective methods for disseminating

emerging knowledge about cancer risk, prevention, diagnosis, treatment (including palliative care), and survivorship to appropriate audiences. NCI will:

- Conduct a portfolio analysis of dissemination and implementation research at NCI and other NIH Institutes and Centers to determine what further research is needed to reduce cancer-related risk factors and improve the quality of care across the full spectrum of cancer interventions.
- Support research to identify effective approaches for communicating the importance of prevention interventions targeting healthy people.
- Investigate and identify the most effective methods of integrating palliative care into clinical practice for cancer patients.

- Investigate cultural tailoring of complex cancer information, including the risks and benefits of participation in clinical trials, cancer prevention and treatment programs, and develop delivery methods to reach underserved populations and populations at risk.
- Support dissemination and implementation research by transdisciplinary teams of scientists and practitioners to develop and/or test conceptual models of dissemination and implementation, and evaluate the outcome of these efforts.

STRATEGIC OBJECTIVE 6

Improve the Quality of Cancer Care

We will support the development and dissemination of quality improvement interventions and measure their success in improving health-related outcomes across the cancer continuum.

As interventions and technologies become more sophisticated, the cancer community must build upon research evidence to continually enhance the quality, safety, and appropriateness of care—including prevention, screening and follow-up, staging and accurate diagnosis, treatment and adjuvant therapy, and systematic follow-up to both prevent and detect recurrence and second cancers. It is also critical to prevent or identify and treat the chronic and other late effects of cancer and its treatment. This will be accomplished through the efforts of public health programs, primary care practitioners, oncologists, and others who care for cancer patients, survivors, and their families.

Desired health outcomes include survival and health-related quality of life. For cancer, high quality care means delivering the full range of evidence-based interventions that are safe, patient-centered, effective (i.e., likely to provide more benefit than harm), timely, efficient, and equitable. Such care must be provided with technical competence and cultural sensitivity and must foster patient choice based on informed decision making.

Research on quality of cancer care includes surveillance, epidemiologic, and cost-effectiveness studies. It includes examining patterns and variation in care among diverse patient populations and provider groups. Quality of care studies also encompass the development of ways to measure how well standards of care are applied in practice and the outcomes of that care. Outcomes include observable intermediate endpoints (tumor shrinkage, for example) and survival as well as outcomes reported by patients and/or caregivers. Stronger scientific evidence for public and private decision making related to care delivery, coverage, purchasing, regulation, and standard setting will enhance the efficiency and quality of cancer care services.

STRATEGY 6.1 — Foster the use of research evidence about patterns of care and care outcomes to develop quality improvement interventions.

Improving care first requires measuring and understanding patterns of care and then building on that understanding to ensure that the best information is used to reduce unwanted variations in care or poor outcomes and enhance the quality and safety of cancer care. NCI will:

- Examine how care varies by age, race, ethnicity, and socioeconomic status as well as the types and causes of adverse health-related quality of life outcomes.
- Identify clinical and organizational factors that affect whether quality improvements are effective, sustainable, and applicable to different care settings.
- Identify quality improvements likely to have the greatest impact on desired outcomes and partner with other Federal organizations and the private sector to implement them.
- Identify ways to tailor therapies and their delivery to maximize outcomes while minimizing adverse effects and to improve treatment follow-up.
- Promote the use of validated care standards and quality measures that enable healthcare providers to better monitor patient care, make treatment decisions, and manage symptoms.

Electronic Health Records Are Essential for Cancer Patient Care

Integrated electronic health records (EHRs) promise to help healthcare providers and their patients achieve quality and continuity in treatment. Cancer patients receive multimodality therapies that require greater access to and tracking of detailed medical data. Clinical trials, which demand intense documentation, must show cost-effectiveness and patient satisfaction in addition to progression-free and overall survival benefits. Today, oncologists are embracing the medical tools of the Information Age, including the electronic medical record, which is the translator and repository of our clinical information gathering.

As oncologists become more focused on cancer screening and prevention and as clinical trials data management becomes automated, the electronic medical record will become indispensable. We will see collaborative online efforts to develop clinical pathways and multidisciplinary plans of care that standardize patient treatment and decision support. All of this will make more evidence-based medicine possible by bringing current scientific knowledge to the oncologist for point-of-care decision making.

STRATEGY 6.2 — Implement advanced information systems and interoperable electronic health records to inform future research and guide clinical practice.

The cancer research enterprise provides a logical venue for developing advanced medical informatics and health information systems that can revolutionize both cancer research and cancer care. New approaches will improve the coordination, integration, and timeliness of care decisions for cancer patients. Electronic health records will enable healthcare providers and clinical trial investigators to make more efficient, informed, and personalized decisions about care and complete the cycle of science from the bedside back to the bench. NCI will:

> Develop a medical informatics infrastructure to link to national epidemiologic databases and to coordinate communication among the multiple participants in cancer care, including primary care practitioners.

- Work with others to implement state-of-the-art information systems to quickly access relevant patient health information for use in research and practice.
- Collaborate with other agencies to ensure that patient medical information is used only in ways that improve care delivery while protecting patient privacy.

STRATEGY 6.3 — Translate symptom management and palliative care research into interventions to improve care for patients and survivors and at the end of life.

A substantial number of patients experience cancer- and treatment-related physical and psychosocial impairments. Pain, depression, and fatigue, alone or in combination, are the most frequently cited symptoms. NCI will:

- Encourage research collaborations across disciplines and care delivery systems to investigate biological mechanisms of cancer- and treatment-related symptoms and impairments.
- Translate research on the biological mechanisms of symptoms to develop more targeted interventions for preventing and treating symptoms that occur at any point along the cancer continuum.
- Expand on new understandings of evidence-based symptom management and palliative care to deliver care to vulnerable, medically underserved, and special populations.
- Provide training to care providers on integrating the latest evidence-based symptom management and palliative care interventions into clinical practice.

"Palliative care"—also called comfort care, supportive care, or symptom management—is care given to improve the quality of life of patients who have a serious or life-threatening disease. Once largely confined to providing comfort to the dying, the field of palliative care has broadened to include the prevention or treatment as early as possible of the symptoms of the disease and the side effects caused by treatment of the disease—including the physical, social, psychological, and spiritual aspects of coping with cancer—over the entire continuum of care.

STRATEGY 6.4—Ensure that the best scientific evidence about quality measures and assessment informs Federal, state, and private sector decision making about cancer care.

As our understanding of what constitutes quality cancer care increases, this knowledge must be used to inform policy making and program development. NCI will:

- Work to improve evidence-based cancer care delivery by strengthening the scientific evidence for public and private decision making on care delivery, coverage, purchasing, regulation, and standard setting.
- Work with the Agency for Healthcare Research and Quality, the Centers for Medicare and Medicaid Services, the Centers for Disease Control and Prevention, and other organizations to identify a core set of cancer quality measures for public reporting, quality improvement, and surveillance that tracks the burden of cancer and the quality of care over time.
- Participate in public and private sector efforts and work with accrediting organizations, professional societies, and healthcare organizations to foster the adoption of evidence-based interventions.

STRATEGY 6.5—Ensure that relevant audiences receive new information about cancer prevention, treatment, and follow-up.

Healthcare providers; people at high risk for cancer; and people who receive a cancer diagnosis, their families, and caregivers all need appropriate and timely information to make informed decisions about prevention, treatment, follow-up, and end-of-life care. As we gain new knowledge about cancer risk and develop evidence-based prevention and treatment interventions, NCI will work to ensure that this information reaches and is used by providers and patients. We will:

- Work in strategic partnerships with advocacy organizations, professional societies, other Federal agencies, the oncology community, and health plans to disseminate research findings and address barriers to their adoption.
- Use diverse media platforms and both contemporary and traditional communication methods that respond to patient needs and support informed decision making at all levels.

STRATEGY 6.6 — Strengthen the methodological basis for evaluating quality improvement efforts.

Developing methods to assess the value, replicability, or adaptation of cancer care quality improvement interventions is a prerequisite to improving clinical care processes. NCI will:

- Assess the effectiveness of existing and new quality of care interventions to inform future efforts.
- Assess the delivery and impact of patient-centered communication across the cancer care continuum. We will employ innovative measurement approaches and study designs to help monitor and track the success of communication efforts over the course of the patient, family, and healthcare provider experience.
- Assess the effectiveness of specific information technologies in improving quality of care.

STRATEGIC OBJECTIVE 7

Improve the Quality of Life for Cancer Patients, Survivors, and Their Families

We will support the development and dissemination of interventions to reduce the adverse effects of cancer diagnosis and treatment and improve health-related outcomes for cancer patients, survivors, and their families.

NCI's Vision to eliminate the suffering and death due to cancer supports the interests of the nearly ten million cancer survivors in the United States today. While the ultimate goal of eliminating cancer entirely continues to be our long-term commitment, the capacity to dramatically reduce the suffering caused by cancer is within our immediate grasp. This is in keeping with the Department of Health and Human Services Healthy People 2010 goal of five-year survival for 70 percent of those diagnosed with cancer. Advances in our ability to detect, treat, and support cancer patients have turned this disease into one that is chronic or readily managed for many and curable for increasing numbers.

We are learning more about the nature and scope of problems encountered by cancer survivors. Research is enabling us to better predict who is at risk for adverse health outcomes and to develop innovative interventions for treatment effects such as fatigue, memory difficulties, mucositis, nausea, and pain. Through clinical trials, investigators are trying to identify genes, proteins, or other biological markers associated with a patient's response to treatment. The ability to use genetic signatures to recognize tumors that are likely to recur after treatment could allow doctors to tailor treatment plans accordingly, sparing patients with good prognoses unnecessary therapy.

Partnering with others will assure appropriate follow-up care and increase adherence to optimal health behaviors among survivors. Understanding the impact of cancer on family members of patients and survivors—many of whom are themselves at increased risk for cancer due to shared cancer-causing genes, lifestyles, or toxic exposures—is also essential to achieving our Vision. As cancer care migrates to the outpatient setting, the economic, physical, and emotional burden on family members is increasing. Research must equip healthcare teams to better prepare family caregivers to manage patients at home while sustaining their own emotional and physical health.

STRATEGY 7.1 — Expand research efforts to understand biologic, physical, psychological, and social mechanisms and their interactions that affect a cancer patient's response to disease, treatment, and recovery.

While research documenting the impact of cancer on patient and survivor health-related outcomes continues to grow, much remains to be learned about who may be at risk for specific disease- or treatment-related sequelae, what factors moderate or mediate risk, and the interaction of these on patient health. Increased understanding of how cancer patients respond to disease, treatment, and recovery will enable the development of interventions to improve quality of life during and after cancer treatment. NCI will:

As people emerge from the physical and emotional intensities of cancer treatment, they often find themselves in a world that is intimately familiar yet forever changed. Typically, few signposts exist to guide these highly personal journeys. Survivorship research cross-cuts the entire research portfolio to help chart and remediate that journey. We strive to adapt treatment to avoid chronic and late effects, ensure appropriate follow-up and post-treatment screening, prevent recurrence, and enable a high quality of life for cancer survivors and their families, friends, and caregivers.

- Strengthen behavioral and epidemiologic studies of cancer and its treatment among patients and survivors examining both negative and positive physiologic and psychosocial effects and their correlates.
- Support research on the biologic and physiologic mechanisms involved in adverse chronic and late effects of both current and new cancer treatments. Using molecular epidemiological research, we will seek to identify the genetic and/or phenotypic markers of susceptibility to treatment-related adverse effects and gene-environment interactions.
- Promote the incorporation of quality-of-life endpoints within NCI-supported clinical trials and enhance the capacity for long-term follow-up of survivor cohorts.
- Collaborate with others to synthesize the research on the role of sociocultural, behavioral, emotional, and spiritual factors in survivor and family outcomes and survivors' adoption of appropriate surveillance and health maintenance behaviors post treatment.

STRATEGY 7.2—Expand the development and use of tools to assess the health-related quality of life of cancer survivors and their family members across the trajectory of care.

Improving patient outcomes will require tools to measure and describe patients' experience of illness, treatment, and recovery. NCI will:

> Support the identification, development, and testing of instruments to assess the health-related quality of life of patients and survivors from diagnosis through the end of life.

> Promote the routine use of standardized instruments at systematic time points across the trajectory of care, including the adoption of newly established criteria for monitoring harmful late effects of cancer treatment.

> Collaborate with other NIH Institutes to support the development of measures and create data banks for evaluating comorbidities to better describe the effects of a cancer diagnosis on long-term health.

> Support the development of measures to assess the impact of a patient's cancer on the health-related quality of life of family members and caregivers.

STRATEGY 7.3—Accelerate intervention research designed to reduce cancer-related acute, chronic, or late morbidity and mortality.

As we learn more about the types and causes of adverse health-related outcomes among cancer patients and survivors, it will be critical that interventions to address them keep pace with our findings. We will:

> Advance research on the most promising and cost-effective interventions to address cancer patient and survivor needs for improved quality of life—e.g., reducing cancer-related symptoms such as distress, pain, and nausea; minimizing post treatment organ dysfunction; treating infertility; promoting healthy practices such as exercise, smoking cessation, and diet change; and addressing individual needs.

> Support research to investigate the impact of well characterized and controlled interventions on appropriate intermediate biomarkers such as immune function, cortisol levels, and hormone levels.

- Advance intervention development that promotes the health and well-being of family members and caregivers as well as interventions that target patients and survivors in minority and medically underserved populations.
- Foster development of screening tools that identify individuals or families at high risk for poor outcomes and support research to assess the impact of such screening on patterns and outcomes of care including health-related quality of life.
- Support the development of personalized treatments for individual patients based on their predisposition for adverse outcomes.

STRATEGY 7.4—Ensure that relevant audiences receive new information, interventions, and best practices for addressing the health needs of survivors and their families.

As information becomes available about the nature of and ways to improve health-related quality of life outcomes for cancer patients, survivors, and their families, we must understand how to effectively disseminate this knowledge and evaluate its impact on care. We will:

- Support the development and dissemination of curricula and standards for delivering effective psychosocial and supportive care for cancer patients and survivors to a broad spectrum of healthcare providers and cancer professionals.
- Collaborate with other Federal and health- or cancer-related professional and nonprofit organizations and advocacy groups to promote the development and dissemination of educational materials across diverse media platforms—e.g., written, CD, audiotape, online, telephone—for family members and healthcare providers.
- Assess health-related information needs and resources through patient, family member, and healthcare provider surveys and use this information to guide the development of educational tools and outreach efforts.

Meeting Survivor Needs at All Life Stages

The experience of cancer and survivorship is not the same for everyone. It is affected by the type of cancer, the stage of diagnosis and treatment, and a person's age at the time of treatment. Along with impressive gains in cancer survival for all age groups have come "late effects," side effects of cancer treatment that only become apparent in the long term. These can include a range of disabilities including learning impairments, sensory impairments such as hearing loss and cataracts, amputations that will compromise mobility, organ system dysfunctions, soft tissue or bone damage, overweight or obesity, and osteoporosis. All cancer survivors have the need to obtain, upon discharge from cancer treatment, a record of all care received and important disease characteristics, along with a follow-up plan for their health care. But in particular, survivors who are diagnosed at significant life stages have specific needs that accompany their transition to a healthy life.

Children

Survivors of cancer diagnosed in childhood may need special assistance to re-enter the classroom setting successfully as well as attention to social development and psychosocial issues. Support groups and services tend to be robust during the treatment period but are less available after the return home. As for late effects, many survivors of childhood cancers are not being transitioned appropriately from pediatric to adult health care settings.

Young Adults

This is a generation which has been lost between older people with cancer and pediatric patients. The current health system is not set up to address young adult concerns about gaining independence, keeping jobs, attracting mates, or having children. Young adults frequently have temporary employment and lack health insurance and a steady relationship with a doctor, making follow-up difficult. Young adult survivors often indicate that they must educate providers about their cancer history and late effects.

Adults

Cancer occurring during the prime and middle years of adulthood may seriously disrupt the survivor's ability to carry out family, social, and work-related responsibilities. They frequently are "sandwiched" between caring for children and aging parents as well as their own disease or late effects of treatment. They may have difficulty re-establishing intimacy in their personal relationships. Adult survivors typically are unable to obtain or increase life or disability insurance and may have difficulty securing mortgages or loans or maintaining employment.

Older Adults

Those diagnosed at age 60 or older comprise the majority of cancer survivors. Many older survivors also have one or more other chronic medical conditions (comorbidities) that can mask signs of cancer recurrence or late effects. They may live alone and lack adequate social and caregiver support or transportation. Limitations on Medicare reimbursement along with out-of-pocket costs are a significant burden for those on fixed incomes.

Late effects are accompanied by issues concerning follow-up care and resources, insurance portability, psychosocial support for the survivor and caregiver, and availability of health information. Electronic health record systems have enormous potential to improve continuity of follow-up care. NCI is exploring collaborative opportunities to ensure that post-treatment care for all survivors reflects emerging understanding of late effects and specific needs, is informed by quality of life research, makes use of advanced technologies, and helps guide standards and policy that promote lifelong wellness.

STRATEGIC OBJECTIVE 8

Overcome Cancer Health Disparities

We will study and identify factors contributing to disparities, develop culturally appropriate approaches, and disseminate interventions to overcome those disparities across the cancer control continuum from disease prevention to end-of-life care.

Overcoming cancer health disparities is one of the best opportunities we have for eliminating the suffering and death due to cancer. Addressing the needs of the medically underserved is a critical component of each of our NCI strategic objectives. Significant progress has been made over the past three decades in understanding, preventing, detecting, diagnosing, and treating cancer and in improving the quality of cancer survivorship and end-of-life care. Sadly, not all Americans are reaping the benefits of this progress.

Because cancer initiation and progression are determined by complex interactions among genetic, behavioral, cultural, social, and environmental factors, some level of health disparity—e.g., higher than average incidence, more rapid disease progression, poorer outcome or survival—can affect anyone. However, several assessments conducted in recent years point to the unequal burden of disease in our society as not just a scientific and medical challenge but also a moral and ethical dilemma for our Nation. Minorities and other underserved populations variously distinguished by race, ethnicity, gender, age, socioeconomic status, geographic location, occupation, and education bear a far greater cancer burden than the general population.

NCI must take the lead in accelerating the dissemination and implementation of interventions to address cancer health disparities. We must establish collaborations and partnerships with public, private, and community organizations to address inequities. We must work more efficiently and effectively with current partners, evaluate the impact of our efforts, and broaden our bases of collaboration. This kind of resource integration provides our best hope of overcoming cancer health disparities.

STRATEGY 8.1 — Understand the factors that cause cancer health disparities.

A first step in eliminating disparities in cancer incidence, treatment, and survival is to understand their underlying causes and contributing factors. NCI will:

- Assemble interdisciplinary teams of scientists and practitioners to further elucidate the complex interplay of social, behavioral, environmental, genetic, public health, and economic factors, as well as political and health system forces, that may contribute to disparities.
- Advance research to identify and investigate race, ethnicity, and socioeconomic status and how they influence trends and rates of cancer incidence and mortality.
- Support efforts to disaggregate large population studies in order to identify geographic areas of high cancer mortality and investigate the complex mechanisms that underlie the disparities identified across various age groups and stages of cancer.

New knowledge in these areas will support continued work with other government, academic, and private organizations to develop effective and appropriate interventions.

STRATEGY 8.2—Work with communities to develop interventions targeted to the specific needs of underserved populations.

Community-based programs like the Community Networks to Reduce Cancer Disparities, the Minority-Based Clinical Oncology Program, NCI-supported Cancer Centers, and other academic centers located in underserved areas are ideal venues for designing and testing interventions. By understanding the health experience of these communities, researchers are able to develop more culturally appropriate and accessible interventions, healthcare providers are more likely to arrange for their patients to participate in cutting-edge clinical research, and cancer patients and people at risk have access to the full range of state-of-the-art cancer services. NCI will:

- Work with community members, leaders, and healthcare providers to implement clinical, correlative, and community research for populations known to bear heavy burdens of cancer and work to ensure broader community participation in clinical trials for patients and healthcare providers.
- Foster the participation of community and academic partners to facilitate the development of education, research, and training programs that will increase access to and use of cancer prevention interventions such as smoking cessation, healthy eating and physical activity and the early detection, diagnosis, and treatment of cancer.

These activities will help to build sustainable alliances with local communities.

Community-Based Research Is Vital for Understanding Health Disparities

Given the complex determinants of health status, the disproportionate burden of disease, and the limited effectiveness of traditional research methods, particularly within underserved communities, more comprehensive and participatory approaches to public health research and practice are essential. Community-based participatory research (CBPR) is a collaborative approach that equitably involves academic, public health, and community partners in the research process. By combining the unique strengths of individuals and groups, CBPR aims to undertake research of importance to the community, with the goal of achieving social change.

STRATEGY 8.3—Provide the knowledge base for and develop interventions to enhance the integration of cancer services for underserved populations.

Despite new technological advances in diagnostic and therapeutic interventions, the complex interplay among behavioral, social, and environmental factors continues to undermine access to cancer services and widen the gap in healthcare disparities. This problem is coupled with escalating healthcare costs and the high numbers of uninsured and underinsured people. Under these conditions, healthcare providers must sometimes make difficult treatment decisions and underserved patient populations are less likely to have access to new advances in cancer prevention, diagnosis, and therapy. To counter this disparity, NCI will:

- Conduct research to discover the most effective ways to address critical gaps in access to care by supporting patient navigator program development and the replication of effective models.
- Determine the best ways to provide culturally appropriate care, taking into account socioeconomics, comorbidities, diagnostic and treatment interventions, survivorship, and end-of-life needs.
- Conduct community-based research to develop strategies for increasing trust and encouraging participation in cancer research.
- Promote an interdisciplinary team approach to accelerate the integration of cancer healthcare services.

These efforts will expand the participation of underserved populations in the Nation's cancer research enterprise and the availability and delivery of associated discoveries.

Patient Navigator Programs Are Key to Cancer Care Integration

"Patient navigation" in cancer care refers to the assistance offered to patients, survivors, families, and caregivers to help them access and chart a course through the healthcare system. Navigators are experienced lay people, social workers, nurses, and others from local communities who are able to communicate credibly with patients. They work with vulnerable or disadvantaged people to help them obtain accurate information on diagnosis and treatment procedures, access to hospitals and clinics, guidance on financial assistance, and help with tracking their records and obtaining prescriptions. In some cases they also arrange for language translation, travel, social support, or religious counseling.

STRATEGY 8.4—Work with others to develop a cadre of researchers and clinicians prepared to effectively address cancer health disparities.

The success of research designed to reduce the disproportionate burden of cancer incidence and mortality in underserved populations will depend on increasing the number of culturally sensitive, well trained investigators. NCI will:

- Support introductory science experiences for minority high school students, individual and institutional fellowships and other college level training programs, career development awards, mentored research fellowships for postdoctoral and junior investigators, and the cross training of non-minority researchers.
- Work with schools of public health, social work, health administration, and medicine to promote health disparities communication and outreach efforts and encourage students to consider health disparities research as a career.
- Support NCI-designated Cancer Centers and Minority-Serving Institutions conducting joint research, training, education, and outreach programs with particular focus on the disproportionate incidence, morbidity, and mortality of cancer in underrepresented minority populations.
- Support studies to understand cultural and behavioral factors that affect the conduct of research and how cancer care is provided and ensure that new insights are used to guide research and inform practice.
- Collaborate with Cancer Centers and grantee institutions to promote training on cancer health disparities issues for healthcare providers and scientists.

A better prepared cadre of researchers and clinicians will help to address the unrecognized and unintentional biases that impede quality cancer care.

STRATEGY 8.5—Develop and work with others to implement innovative, educationally and culturally appropriate approaches for disseminating information on research results to underserved populations.

Communication, outreach, and information dissemination with underserved populations requires innovative approaches and community involvement. NCI will:

- Use knowledge gained from health literacy and risk perception research to develop and implement plans for disseminating new interventions and relevant scientific information.

- Ensure that NCI publications and other communications tools are reviewed for cultural appropriateness and adapted as needed.
- Ensure comprehensive coverage of NCI publications in communications targeted to underserved populations.
- Team with health disparity experts, cancer advocacy groups, and cancer education specialists to disseminate consistent, current, and accurate information.
- Partner with the minority and national media to reach their constituents with timely and accurate health messages.
- Support public workshops and focused dissemination efforts to address the many needs related to health disparities.

Partnerships between NCI and other public, private, and non-traditional organizations will increasingly improve NCI's communication, outreach, and dissemination efforts.

NCI's Cancer Information Service Partners to Reach the Underserved

The NCI Cancer Information Service (CIS) is a national resource for information and education about cancer and a leader in translating cancer information into language the public can easily understand. Through its Partnership Program, the CIS reaches the medically underserved, including minority groups and people with limited access to health information and services throughout the United States and its territories.

CIS works with other agencies and organizations that have an established presence in the state or region and are trusted within their communities. In 2004, the CIS collaborated with over 100 partners to reach underserved African American populations with information and resources on breast and cervical cancer, clinical trials, tobacco control, and general cancer awareness. Working with others, the CIS is able to work across the country to reach those most in need with vital cancer information and services.

STRATEGY 8.6—Examine the role of health policy in reducing and eliminating cancer health disparities.

Strong evidence-based health policies can provide a critical link in helping to understand and overcome cancer health disparities. However, additional research is needed to understand factors affecting the development and implementation of health policies, their differential impact and unintended consequences, and variations in their enforcement. NCI will identify gaps in our current knowledge and understanding, delineate areas in which further research is needed, and recommend effective policy strategies and programs for reducing cancer health disparities. NCI will:

- Examine the interrelationships between cancer control policies and social, cultural, and environmental influences within specific populations.
- Assess the cultural appropriateness of evidence-based policies as they apply to various population groups.
- Examine the differential impact of policies on health systems, organizations, and institutions with multiple local, state, and national programs.
- Build collaborations among researchers from diverse disciplines, academic settings, service delivery environments, and global communities to examine the issues of appropriateness, impact, translation, and dissemination of evidence-based health policies.
- Support the dissemination and adoption of innovative approaches to policy issues concerning insurability and the challenges faced by the uninsured and underinsured.
- Collaborate with U.S. and international stakeholders to identify the types of data and data training needed by decision makers to help influence policy.

These investments will improve the effectiveness of policy decisions aimed at reducing cancer risk and incidence, facilitating early cancer treatment, and increasing survival rates among those who suffer disproportionately from cancer.

Monitoring and Reporting Progress

Measuring progress in biomedical research requires innovative methodologies that go beyond the approaches typically used for other kinds of program evaluation. The serendipitous nature of research, the type of goals and objectives that are appropriate for research endeavors, the duration of time required for research goals to be achieved, and the difficulties in demonstrating cause and effect are all characteristics that present challenges when evaluating biomedical research. And just as no single scientific discipline or approach is suitable for addressing the full spectrum of topics represented in NCI-sponsored research, no single evaluative approach can capture all aspects of progress in cancer research. Therefore, it is important to use multiple methods in parallel to provide converging evidence of our progress.

By defining our strategic objectives in this plan, we are indicating what we believe will be required of NCI to lead the Nation in achieving a future when people no longer suffer and die due to cancer and incidence is dramatically reduced. As we proceed with the implementation of our strategies for achieving these objectives, we will continually monitor the outcomes of our programs as well as the Nation's progress toward this Vision.

To monitor the progress of NCI research programs …

We will use a number of indicators and sources. Grantee progress reports will provide information about individual research projects and about our progress in specific scientific areas. Larger programs and initiatives which focus on research in strategic areas will be evaluated using metrics for specific scientific objectives. We will also conduct portfolio reviews and analyses, monitor funding trends, and evaluate needs and opportunities through peer review. This information will be used on an ongoing basis to guide the allocation of resources and maximize the impact of our efforts. This progress will be communicated in documents such as the NCI Director's annual report, *The Nation's Progress in Cancer Research*[1]; reports of program evaluations; the annual NCI Congressional Budget Justification[2]; the *NCI Fact Book*; and the *NCI Cancer Bulletin*[3]. In addition, NCI's Cancer Research Portfolio database and Web site[4] provide information on nearly all NCI research projects and initiatives.

[1] cancer.gov/nci-annual-report
[2] cancer.gov/admin/fmb
[3] cancer.gov/ncicancerbulletin
[4] researchportfolio.cancer.gov

To monitor the Nation's progress in eliminating the suffering and death due to cancer …

The NCI Surveillance, Epidemiology, and End Results (SEER)[5] program will continue to use a number of quantitative measures such as cancer incidence, prevalence, mortality, morbidity, and survival rates as well as shifts in stage at diagnosis. SEER data are a major source for *The Annual Report to the Nation on the Status of Cancer*[6], a collaborative effort among the American Cancer Society (ACS), the Centers for Disease Control and Prevention (CDC), NCI, and the North American Association of Central Cancer Registries. The report provides updated information on cancer incidence, mortality, and other trends in the United States. NCI also publishes the *Cancer Progress Report*[7] to provide a biannual update that identifies gains made and further work needed in cancer prevention, early detection, diagnosis, treatment, life after cancer, and end of life. The information for this report is gathered through a collaborative effort with other agencies and organizations including CDC and ACS.

While there are characteristics of biomedical research that make monitoring and reporting progress a challenging task, we will continue to find ways to gauge return on investment and ensure that the Nation's resources are used efficiently, effectively, and economically. By employing multiple methods for monitoring progress, we will assess both NCI's success in achieving the strategic objectives in this plan and the Nation's progress toward our ultimate Vision. Through the hard work and dedication of all members of the cancer research, public health, medical, and advocacy communities, we will realize the ultimate success indicator—the elimination of suffering and death due to cancer.

[5] seer.cancer.gov

[6] seer.cancer.gov/report_to_nation

[7] progressreport.cancer.gov

Michelle Bennett, Kishor Bhatia, Diane Bronzert, Karen Colbert, Susan Erickson, Tracy Lively, Catherine McClave, Kate McNeill, Michael Miller, Isabel Otero, Anita Ousley, Anne Ryan **Office of Communications:** Nelvis Castro, Donna Bonner, Del Harrod, Paul LaMasters, Anne Lubenow, Peter Garrett, Rick Manrow, Julie Cheh, Jane Lockmuller **Office of the Director:** Dotty Foellmer, Kathleen Schlom, Sarah Birckhead, Sandy Koeneman, Bruce Clark, Mieko Togashi, Ann Bodmer **Our Advisory Groups:** President's Cancer Panel LaSalle Leffall, Lance Armstrong, Margaret Kripke National Cancer Advisory Board Samir Abu-Ghazaleh, James Armitage, Moon Chen, Kenneth Cowan, Jean deKernion, Ralph Freedman, James French, Kathy Giusti, David Koch, Eric Lander, Diana Lopez, Arthur Nienhuis, Marlys Popma, Franklyn Prendergast, Carolyn Runowicz, Lydia Ryan, Daniel Von Hoff Board of Scientific Advisors David Alberts, Hoda Anton-Culver, Kirby Bland, Esther Chang, Raymond Dubois, H. Shelton Earp, Kathleen Foley, Sanjiv Gambhir, Patricia Ganz, Joe Gray, William Hait, Mary Hendrix, Susan Horwitz, Hedvig Hricak, Eric Hunter, Paula Kim, Kenneth Kinzler, Michael Link, Christopher Logothetis, Lynn Matrisian, Edith Perez, John Potter, Mack Roach, Richard Schilsky, Ellen Sigal, Margaret Spitz, Jane Weeks, Robert Young Board of Scientific Counselors Stephen Benkovic, Christine Biron, Olivera Finn, Sankar Ghosh, Michael Gould, James Haber, Katherine Jones, Michael Karin, Laimonis Laimins, Dan Littman, Guillermina Lozano, Frank Rauscher, Martine Roussel, Leona Samsono, Robert Siliciano, Harinder Singh, Ronald Swanstrom, Joseph Testa, Thea Tlsty, Jeffrey Trent, Paul Ts'o, Cheryl Walker, Teresa Wang, Jerry Workman, Leslie Bernstein, Martin Blaser, David Carbone, Esteban Celis, Leland Chung, Scott Davis, Barbara Gilchrest, Stanley Hamilton, Richard Hoppe, Elizabeth Jaffee, Bruce Korf, Theodore Lawrence, Susan Leigh, Maria Martinez, Susan Mayne, Daniel Medina, Monica Morrow, Andrew Olshan, Timothy Rebbeck, Eric Rowinsky, Charles Sawyers, David Scadden, Steven Self, Paul Sondel, Margaret Tempero, Ann Thor Director's Consumer Liaison Group Margaret Anthony, Vernal Branch, William Bro, Lourie Campos, Nancy Davenport-Ennis, Bobbi DeCordova-Hanks, Beverly Laird, Sylvia Ramos, Eric Rosenthal, Mary Scroggins, Sue Sumpter, Douglas Ulman, Marisa Weiss, Celeste Whitewolf, James Williams **Many Others:** People who responded to our NCI Listens and Learns questions, Participants in Think Tanks in Cancer Biology, Participants in annual conferences on Cancer Survivorship, Participants in President's Cancer Panel meetings, Participants in the Clinical Trials Working Group of the National Cancer Advisory Board, Members of the Planning and Budget Subcommittee of the National Cancer Advisory Board, Progress review group members and roundtable participants, Numerous others who have provided formal and informal input about future directions to NCI staff

NATIONAL® CANCER INSTITUTE

NIH Publication No. 06-5773
Printed January 2006