

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



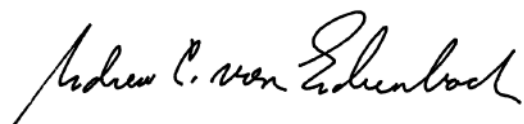
## Director's Message

**E**arly 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 policy-makers 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.

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



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

## Our Strategic Objectives

### To Preempt Cancer at Every Opportunity

#### Understand the Causes and Mechanisms of Cancer . . . . . 6

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.

#### Accelerate Progress in Cancer Prevention . . . . . 18

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.

#### Improve Early Detection and Diagnosis . . . . . 28

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

#### Develop Effective and Efficient Treatments . . . . . 38

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

#### Understand the Factors that Influence Cancer Outcomes . . . . . 48

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.

#### Improve the Quality of Cancer Care . . . . . 56

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

#### Improve the Quality of Life for Cancer Patients, Survivors, and Their Families . . . . . 62

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.

#### Overcome Cancer Health Disparities . . . . . 68

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.

### Measuring and Reporting Progress . . . . . 75



**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<sup>1</sup>, 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.



<sup>1</sup> 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.

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.

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.

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:

- > 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.

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.

**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.

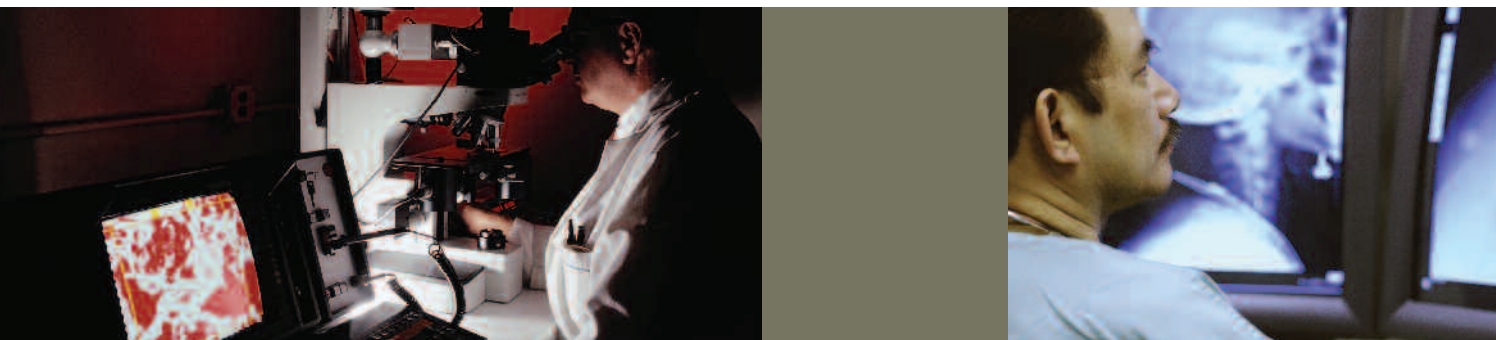
Cancer remains one of the most complicated and difficult diseases to diagnose and manage. A systems approach is needed to both integrate information and data and meld the cultures and disciplines needed in this enterprise. NCI will support a broad set of interactions and efforts, both within NCI and 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.

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