Summary of Research Activities by Disease Categories

Cancer

By the late 1970s, it was well known that genes from viruses could rapidly transform normal cells into cancer cells and that the viruses acquired these genes from the genomes of the animals and birds that they infected. In 1982, three separate laboratories all cloned the first human cancer-causing gene, called an "oncogene." This discovery was the result of the laborious process of testing increasingly smaller pieces of DNA from a cancer cell for the ability to cause cancer. Subsequent studies confirmed that the oncogene was a version of a gene called ras, which had been incorporated into the mouse genome from a mouse virus. The ras gene in the mouse virus had a single genetic change that caused it to induce uncontrolled growth that resulted in cancer. This elegant work confirmed what had previously been just a notion—that cancer was a disease of altered genes. This finding began the era of modern molecular cancer research and treatment[1].

Introduction

Cells are the building blocks of all living things. Normal cells multiply in an orderly way and die when no longer needed. Cancer can be described as uncontrolled growth of abnormal cells from almost any organ or tissue within the body. The process that leads to cell death is often blocked in cancer cells. Cancer cells can invade nearby tissues and spread to other parts of the body. Because it takes so many forms and occurs in so many parts of the body, cancer should be thought of not as a single disease but as a complex set of diseases that must be studied from multiple perspectives.

The National Institutes of Health's (NIH's) strategic approach to cancer research focuses on understanding the causes and mechanisms of cancer; accelerating progress in cancer prevention; improving early detection and diagnosis; developing effective and efficient treatments; understanding factors that influence cancer outcomes; improving the quality of cancer care; improving the quality of life for cancer patients, survivors, and their families; and overcoming cancer health disparities.

NIH also coordinates transdisciplinary translational research designed to realize a vision of personalized medicine. As this vision evolves, doctors will be able to use detailed information about an individual's tumor and employ molecular and clinical data to guide the selection of therapies or preventive measures that are most likely to be safe and effective for that person. Personalized medicine promises to improve quality of life for cancer survivors, minimize adverse side effects of therapy, and reduce disparities among populations currently experiencing an excess burden of cancer.

Several examples illustrate the types of research advances and promising new initiatives achieved by NIH scientists and grantees. For example, Gardasil®, the first vaccine to prevent cervical cancer induced by human papillomavirus (HPV), has the potential to save over 200,000 women's lives worldwide each year, including 5,000 U.S. women's lives. In another example, using whole-genome scans, the Cancer Genetic Markers of Susceptibility project has pinpointed common genetic variants associated with increased risk of breast and prostate cancers. In addition, the National Cancer Institute (NCI) and the National Institute of Environmental Health Sciences (NIEHS) have launched the Breast Cancer and Environment Research Centers to study the impact of prenatal-to-adult environmental exposures that may predispose a woman to breast cancer.

[1] For more information, see http://www.nature.com/milestones/milecancer/full/milecancer17.html

Cancer research is conducted by a number of NIH Institutes and Centers (ICs); most of the research investment is committed to NCI programs. NCI's two intramural divisions conduct basic, translational, clinical, and population research, making fundamental discoveries related to cancer causes and mechanisms, genetics, and host immunological and other responses to cancer and rapidly translating those findings into novel preventive and detection methods and therapies. Five NCI extramural divisions support research carried out at nearly 650 universities, hospitals, cancer centers, specialized networks and research consortia, and other sites throughout the United States and in more than 20 other countries. In addition, NCI provides infrastructure to help the greater cancer research community take advantage of the potential benefits of emerging technologies (e.g., genomics, proteomics, bioinformatics, and molecular imaging).

Cancer research conducted or supported by other NIH ICs is wide ranging and often is coordinated with NCI programs and grantees—for example, the Surveillance, Epidemiology, and End Results (SEER) program (a source of information on cancer incidence and survival in the United States) and the nationwide network of NCI-funded Comprehensive Cancer Centers. Examples of cancer research within other ICs include:

- National Institute on Aging (NIA) research on prostate and skin cancers and the biology of aging as it relates to cancer
- NIEHS research on the effects of biological, chemical, or physical agents on human health
- National Heart, Lung, and Blood Institute (NHLBI) research on blood-related cancers and support for breast, colorectal, and reproductive cancer as the administrative coordinator of the NIH Women's Health Initiative
- National Institute of Dental and Craniofacial Research (NIDCR) research on head and neck cancers
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) research on liver, prostate, kidney, colorectal, and bladder cancers
- National Institute of Allergy and Infectious Diseases (NIAID) technology development in support of cancer research, diagnosis, and therapy and studies of the role of viruses in cancer
- National Institute of Neurological Disorders and Stroke (NINDS) research on brain, spinal cord, and pituitary cancers
- National Institute of Nursing Research (NINR) HIV/AIDS and Oncology program
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) research on breast and reproductive cancers
- National Institute of General Medical Sciences (NIGMS) cancer-related basic biomedical research
- National Institute of Biomedical Imaging and Bioengineering (NIBIB) imaging and bioinformatics technology development in areas that are vital to cancer research
- National Institute on Drug Abuse (NIDA) research on treatments for tobacco addiction serving as cancer prevention

Burden of Illness and Related Health Statistics

Because cancer is the second leading cause of death in the United States and the economic cost of cancer in 2005 was estimated at over $200 billion (including $74 billion in direct health care costs and over $135 billion in indirect costs associated with lost productivity due to illness and premature death), cancer research is a major NIH priority[2]. Although significant progress has been made toward reducing the burden of cancer in America, cancer

[2] For more information, see http://obf.cancer.gov/financial/attachments/06Factbk.pdf

remains a leading cause of death, second only to heart disease—one of every four deaths is due to cancer[3], [4]. The American Cancer Society estimated that, in 2007, there were about 1,444,920 new diagnoses of invasive cancer and 564,830 Americans died of cancer[5]. Moreover, the World Cancer Report indicates that cancer rates are set to increase at an alarming rate globally — specifically, they could further increase by 50% to 15 million new cases in the year 2020.

One sign of progress is that U.S. death rates for the most common cancers and for all cancers combined have decreased significantly since 1995[6]. However, the annual number of cancer diagnoses is expected to almost double over the next 50 years, from 1.4 million to 2.6 million. Increasing numbers of Americans are surviving cancer. NIH estimated that, on January 1, 2003, 10.5 million living Americans had a history of invasive cancer[7]. [7]These numbers are likely to increase because of the anticipated growth and aging of the U.S. population[8].

The most common cause of cancer-related death in the United States is lung cancer. The three most common cancers among men are prostate cancer, lung cancer, and colon cancer. For women, the three most frequently occurring cancers are breast cancer, lung cancer, and colon cancer[9].

Significant disparities in the U.S. burden of cancer have been documented through literature reviews, program reviews, and ongoing research. These disparities are discussed in the section "Minority Health and Health Disparities" later in this chapter.

NIH Funding for Cancer Research

In FYs 2006 and 2007, NIH funding for cancer research was $5.575 billion and $5.643 billion respectively. The table at the end of this chapter indicates some of the research areas involved in this investment (see "Estimates of Funding for Various Diseases, Conditions, and Research Areas").

Summary of NIH Activities

Across NIH, cancer research activities are focused on two overarching goals: preempting cancer at every opportunity and ensuring the best outcomes for all. Specific objectives related to these goals include:

Preempting cancer at every opportunity:

- Understanding the causes and mechanisms of cancer
- Accelerating progress in cancer prevention
- Improving early detection and diagnosis

[3] For more information, see http://www.cancer.org.

[4] For more information, see http://www.cdc.gov/nccdphp/burdenbook2004/index.htm

[5] American Cancer Society, 2005.

[6] NCI, 2006.

[7] For more information, see http://seer.cancer.gov/csr/1975_2003

[8] Edwards BK, et al. *Cancer* 2002;94:2766-92, PMID: 12173348

[9] NCI, 2006.

- Developing effective and efficient treatments

Ensuring the best outcomes for all:

- Understanding the factors that influence cancer outcomes
- Improving the quality of cancer care
- Improving quality of life for cancer patients, survivors, and their families
- Overcoming disparities in cancer prevention, diagnosis, treatment, and outcomes

NIH is also exploiting the potential of emerging technologies (e.g., molecular imaging, nanotechnology, and bioinformatics) in cancer research and care and is building the research infrastructure needed to expand knowledge and put new insights into practice.

Preempting Cancer at Every Opportunity

Understanding the Causes and Mechanisms of Cancer

Research that improves our understanding of the causes and mechanisms of cancer—from identifying novel risk factors to elucidating the processes of metastasis (the spread of cancer from the primary tumor site)—is essential to our ability to develop and apply interventions to preempt cancer's initiation and progression. NIH's plan for deciphering the causes and mechanisms of cancer includes studies in molecular epidemiology to define complex risk factors, research on the tumor macroenvironment and microenvironment, understanding the role of altered gene expression in cancer progression and exploring the roles of susceptibility genes in cancer risk and initiation.

A primary challenge for NIH is dissecting the molecular basis of cancer. The Cancer Genome Atlas (TCGA) is developing a comprehensive catalogue of the genetic changes that occur in cancers. The genomic information generated by TCGA could fuel rapid advances in cancer research and suggest new therapeutic targets. It could also suggest new ways to categorize tumors, which might allow clinical trials to focus on those patients who are most likely to respond to specific treatments. **The Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments (TARGET)** initiative identifies and validates therapeutic targets for childhood cancers beginning with acute lymphoblastic leukemia and neuroblastoma.

Genetic susceptibility to cancer and cancer risk associated with environmental exposures are also important research topics. Using powerful new technologies to scan the entire human genome, NIH is conducting genome-wide association studies to identify unsuspected genetic variants associated with cancer risk. The Cancer Genetic Markers of Susceptibility (CGEMS) project, for example, is designed to identify genes that increase the risk of breast and prostate cancers. Similar efforts are directed at cancers of the pancreas, bladder, lung, and other organs. The results of these genome-wide studies promise to provide novel strategies for cancer detection, prevention, and treatment.

Another major NIH initiative is the Sister Study, which is investigating environmental and genetic risk factors for breast cancer. This study involves a cohort of 50,000 sisters of women who have had breast cancer. These unaffected sisters are being followed over time, with periodic health updates. The women who develop breast cancer during the follow-up period will be compared with those who remained healthy to identify factors associated with increased cancer risk. NIH is also supporting a network of Breast Cancer and Environment Research Centers (BCERCs) to study the impact of prenatal to adult environmental exposures that may predispose a woman to breast cancer. One of the goals of the BCERCs is to develop public health messages to educate young girls and women who are at high risk of breast cancer about the role of specific environmental stressors in breast cancer

and how to reduce exposures to those stressors.

Other research into the causes and mechanisms of cancer has revealed that tumors function like organs, comprising many interdependent cell types that contribute to tumor development and progression. The relationship between tumors and their surrounding cellular environment evolves over time, strongly influencing tumor progression, metastatic potential, and responsiveness to treatment. The Tumor Microenvironment Network is a new NIH program focused on expanding our understanding of the role of the microenvironment in which a tumor originates and the critical role it plays during tumor development, progression, and metastasis.

Furthermore, interest is growing in the scientific community about the relationship between inflammation and cancer. NIH is actively pursuing research on the linkages between carcinogenesis and alterations in the microenvironment induced by inflammation. Inflammation is a response to acute tissue damage, whether resulting from physical injury, infection, exposure to toxins, or other types of trauma. Current research on inflammation suggests that pro-inflammatory conditions contribute to the development of several types of cancer, including lung, stomach, and liver cancers, and may lead to new treatment approaches.

Another area of research focus at NIH is the interface between aging and cancer. As part of an interagency collaborative effort, eight NCI-designated Cancer Centers are conducting studies on the biology of aging and cancer and addressing questions related to cancer prevention, treatment, and survivorship in older patients. This research will help provide insights into why cancer occurs more frequently in older people, whether cancer behaves differently in older adults than in younger people, whether older patients respond differently to treatment, and how prevention and screening services should be adapted for this population.

Angiogenesis–the growth of new blood vessels–is required at a certain point for tumors to continue to grow beyond a size at which they begin to need their own blood supply. Thus, blockade of angiogenesis can prevent tumor growth. The NIH Trans-Institute Angiogenesis Research Program funds promising angiogenesis research. The program's multidisciplinary approach fosters data exchange and resource sharing among vascular biology and angiogenesis researchers from different disease disciplines. A number of new angiogenesis inhibitors are currently being developed, including several in late-stage clinical trials.

Systems biology and systems genetics are also promising new fields of study that will increase our understanding of the causes and mechanisms of cancer. These disciplines focus on biological and genetic networks that can be measured, modeled, and manipulated rather than focusing on the individual components. Because this research requires multidisciplinary teams of experts in biology, medicine, engineering, mathematics, and computer science, NIH launched the Integrative Cancer Biology Program (ICBP) to develop a framework for these activities. The ICBP has funded nine integrative biology centers around the United States to provide the nucleus for the design and validation of computational and mathematical models of cancer. Networks of genes can be found and their associations with cancer tested and quantified, and parallel association studies can be conducted in relevant human populations.

NIH is expanding its research portfolio related to the basic biology of tumor stem cells (also referred to as tumor-initiating cells). Tumor stem cells may be responsible for the recurrence of malignancy in some cancers. These cells are often resistant to standard chemotherapeutic agents but may contain unique target molecules that may allow their eradication with novel molecular therapeutics. Progress has been made in identifying tumor stem cells in multiple myeloma, acute myelogenous leukemia, and breast cancer.

Accelerating Progress in Cancer Prevention

Current research efforts into preventing cancer focus on modifying behaviors that increase risk, mitigating the

influence of genetic and environmental risk factors, and interrupting the cancer process 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 in precancerous lesions 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 that contribute to cancer susceptibility.

A major step forward in our efforts to prevent cancer has been the development of vaccines that target HPV. Persistent infection with HPV is recognized as the major cause of cervical cancer. Gardasil®, a U.S. Food and Drug Administration (FDA)-approved vaccine against HPV types 6, 11, 16, and 18–the viral types that cause approximately 70 percent of cervical cancers and 90 percent of genital warts–is now available. Other similar vaccines against HPV types 16 and 18 and/or additional subtypes are in development. These vaccines have the potential to save thousands of women's lives annually in the United States and several hundred thousand more each year worldwide. All of these vaccines resulted directly from epidemiological, basic, and preclinical research discoveries, as well as the development of a prototype HPV vaccine, by NIH scientists.

Another area of focus in cancer prevention is cancer's relationship with diet and obesity. In its 2006-2007 Annual Report, the President's Cancer Panel cites evidence that as many as one-third of the nearly 600,000 yearly cancer deaths in the United States can be attributed to unhealthy diets and obesity. In an effort to reduce the cancer incidence, morbidity, and mortality associated with obesity, low physical activity, and poor diet, NIH has funded the Transdisciplinary Research on Energetics and Cancer (TREC) research centers, which foster collaboration among transdisciplinary teams of scientists. The TREC research centers are studying factors that lead to obesity and the mechanisms by which obesity increases the risk of cancer. The TREC initiative is connecting with a number of established initiatives in the area of diet, physical activity, and weight and is integrated with the NIH Obesity Research Task Force Strategic Plan.

Because most cases of lung cancer are caused by tobacco use and are, therefore, preventable, multiple NIH Institutes have co-funded seven Transdisciplinary Tobacco Use Research Centers (TTURCs), which seek to identify familial, early childhood, and lifetime psychosocial pathways associated with smoking initiation, use, cessation, and patterns of dependence. Research on the genetics of addiction, physiological biomarkers, and advanced imaging techniques should allow the development of individualized and community approaches to the prevention and treatment of tobacco-related diseases. The TTURC model demonstrates the feasibility and benefits of scientific collaboration across disciplines and public-private partnerships.

We now know that the environment and behavioral lifestyles can play a critical role in the development of cancer. In fact, it was this discovery that led to a public health success story in the 20th century–the reduction in tobacco use and related diseases. By the mid-1950s, the mysterious and alarming epidemic in lung cancer, a disease that was almost nonexistent in 1900, was linked to smoking behavior. In the last decade, overall cancer death rates have dropped for the first time in a century, driven largely by the dramatic reduction in male smoking from 47 percent in the 1960s to less than 23 percent today. About 40 percent of this drop in overall cancer rates has been credited to the dramatic reduction in male smoking and male lung cancer deaths since 1991 (more than 146,000 fewer deaths during 1991 to 2003 alone). This success has been due to public-private partnerships and is also a trans-HHS victory, as significant research investments have been made over the last 50 years by NCI, NHLBI, NIDA, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the John E. Fogarty International Center (FIC), the Centers for Disease Control and Prevention (CDC), and the Agency for Healthcare Research and Quality (AHRQ).

Without these investments, 40 million Americans might still be smoking today, hundreds of thousands of them would have prematurely of a tobacco-related disease, and billions of dollars would have been spent on their treatment[10].

The NIH-supported Community Clinical Oncology Program (CCOP) provides a network for greater participation in clinical trials on cancer prevention and treatment. Over the past 23 years, more than 200,000 people have enrolled in clinical trials involving CCOP investigators and institutions. One example is the Study of Tamoxifen and Raloxifene (STAR), which compared the drug raloxifene with the drug tamoxifen in reducing invasive breast cancer in high-risk postmenopausal women. The initial results from STAR indicate that raloxifene is as effective as tamoxifen with fewer side effects. The FDA Oncology Drug Advisory Committee has recommended approval of raloxifene for breast cancer prevention.

Improving Early Detection and Diagnosis

Detecting and diagnosing tumors early in the disease process, before the tumor becomes invasive and metastatic, can dramatically improve a patient's odds for successful treatment and survival and prevent a large proportion of cancer deaths. Therefore, NIH seeks to accelerate the translation of basic research findings into sophisticated, minimally invasive procedures that harness imaging, genomic, proteomic, nanotechnology, and other advanced early-detection and diagnostic techniques.

One NIH effort in the area of early detection is the National Lung Screening Trial (NLST), which is comparing two ways of detecting lung cancer–spiral computed tomography (CT) scans and standard chest X-rays. This study aims to answer the important question whether deaths from lung cancer can be reduced through the use of CT screening. Research has shown that spiral CT is capable of detecting not only smaller lung abnormalities, but also more lung cancers than chest x-ray. However, most of the lung abnormalities seen on screening spiral CTs are not cancer. Moreover, it is not known if finding these lung abnormalities will actually benefit people by lowering deaths from lung cancer. NLST is designed to scientifically answer the question of which screening test will better reduce lung cancer deaths and make meaningful recommendations for public policy.

Molecular profiling is an ongoing effort at NIH, from work at the bench to larger initiatives. In the area of molecular diagnostics, NIH has formed the Early Detection Research Network to bring a collaborative approach to the discovery, development, and validation of early-detection biomarkers for clinical application. Another NIH program, the Strategic Partnering to Evaluate Cancer Signatures program, focuses on confirming, evaluating, and refining "signatures" derived from the molecular analysis of tumors (i.e., biomarkers detection) to improve patient management and outcomes. In addition, the Cancer Genome Anatomy Project (CGAP) focuses on determining the gene expression profiles of normal, precancerous, and cancerous cells to improve detection, diagnosis, and treatment. The CGAP Web site makes tools for genomic analysis available to researchers worldwide.

Yet another area of research that holds promise for advancing molecular diagnostics is proteomics–the study of complex arrays of proteins produced by cells and tissues. The completion of the Human Genome Project in 2003 has been a major catalyst for proteomics research, and NIH has taken a leading role in facilitating the translation of proteomics from laboratory research to clinical application through its Clinical Proteomic Technologies Initiative for Cancer. The overall objective of this initiative is to build the foundation of technologies (assessment, optimization, and development), data, reagents and reference materials, computational analysis tools, and the infrastructure needed to systematically advance our understanding of protein biology in cancer and accelerate basic science research and the development of clinical applications.

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[10] Thun MJ, Jemal A. Tobacco Control 2006;15:345-7, PMID: 16998161

The first product of an NIH-funded research project to integrate new technologies into a reliable clinical protocol to improve oral cancer detection has reached the market. Researchers report success using a customized optical device that allows dentists to visualize in a completely new way whether a patient might have a developing oral cancer. Deviations from the natural fluorescence of healthy tissue may indicate the presence of developing tumor cells. Health care providers can shine a light onto a suspicious sore in the mouth, look through an attached eyepiece, and check for changes in color. The instrument is an effective aid in screening and can guide surgeons when removing tissue for biopsies.

Developing Effective and Efficient Treatments

Developing more effective, more efficient, and less toxic cancer treatments is at the heart of the NIH cancer research agenda. A strong understanding of the fundamental mechanisms leading to cancer development, progression, and metastasis will dramatically improve our ability to identify key biochemical pathways in the disease process as targets for treatment. Acceleration of target validation and the development of new treatment modalities will be possible through recent advances in biomedical science and technology. Rapid translation from development to delivery will ensure that promising treatments move safely and efficiently from preclinical investigation through late-stage clinical trials and into clinical practice. NIH is taking a multipronged approach to developing new therapies for cancer.

One innovative initiative, the NCI Experimental Therapeutics Program (NExT), safely shortens the timeline for moving anticancer drugs from the laboratory to the clinic by combining NIH expertise in drug development with state-of-the art research facilities. This program takes advantage of new FDA guidelines that allow human trials, referred to as “Phase 0” or “Early Phase I” trials, to proceed before traditional, expensive, time-consuming drug development steps have occurred. The first Phase 0 study has been successfully completed, demonstrating that this new approach can reduce the number of patients required for an early clinical study and shorten the time necessary to gather critical drug development information.

Another NIH program, the Cancer Imaging Program (CIP), supports cancer-related basic, translational, and clinical research in imaging sciences. CIP initiatives include the development and delivery of image-dependent interventions for malignant and premalignant conditions; standardized models for the design of clinical trials that use imaging technologies; development of emerging imaging technologies, including nanotechnology, proteomics, and high-throughput screening; and development of imaging methods for cancer detection and treatment and for monitoring responses to therapy.

In addition, NIH’s Radiation Research Program (RRP) evaluates the effectiveness of radiation research conducted by grantees. The RRP coordinates its activities with other radiation research programs at NIH, other Federal agencies, and national and international research organizations. Currently, major clinical trials are evaluating radiation therapy dose escalation, as well as novel combinations of chemotherapy with concomitant boost radiation therapy, in non-small cell lung cancer (NSCLC).

Marshalling the exquisite specificity of the immune system to selectively target cancer cells without harming normal cells is another focus of cancer treatment research at NIH. The Cancer Vaccine and Immunotherapy Program is evaluating therapeutic cancer vaccines aimed at antigens that are unique to or overexpressed by cancer cells. Other approaches under evaluation include immunotherapy with T lymphocytes that specifically kill cancer cells, monoclonal antibodies and immunotoxins that target cancer cells, and the use of cytokines that boost the body’s ability to fight cancer. These a pproaches may be used in combination with conventional treatments for cancer, such as chemotherapy and radiotherapy.

NIH launched the Comparative Oncology Program (COP) in an effort to improve the translational research process. Its mission was to provide an integrated mechanism by which naturally occurring cancers in pet dogs could be used to generate new information about cancer, translate biological concepts towards clinical application, and bring novel therapeutic options to the management of human cancers. As part of this effort, COP has established a multi-center collaborative network of extramural comparative oncology programs that have completed three clinical trials this year and plans to initiate five additional trials.

Ensuring the Best Outcomes for All

Research on the quality of cancer care is essential to ensuring the best outcomes for all who may be affected by cancer. Research in this area can include surveillance as well as epidemiological and cost-effectiveness studies. In addition, quality-of-life research increases our understanding of the impact of cancer on patients, survivors, and their family members–many of whom are themselves at increased risk for cancer due to shared cancer-causing genes, life styles, or environmental exposures. Dissemination research helps ensure that the knowledge gained through NIH-supported research is appropriately and effectively communicated to health care providers, policymakers, and the public. An additional goal related to ensuring the best outcomes for all overcoming health disparities in cancer incidence and outcomes is described in a later section of this chapter (see "Minority Health and Health Disparities").

NIH is currently engaged in making cancer a working model for quality-of-care research and the translation of the findings of this research into practice. To this end, several collaborative projects have been initiated: (1) an interagency working committee, The Quality of Cancer Care Committee, which has fostered collaborative projects directly involving the Health Resources and Services Administration, the Centers for Medicare and Medicaid Services, and the Department of Veterans Affairs; (2) the National Quality Forum, a major public-private partnership, to identify core measures of cancer care quality; (3) research on outcomes measurement by the Cancer Outcomes Measurement Working Group and the Cancer Care Outcomes Research and Surveillance Consortium; (4) studies on improving the quality of cancer communications; and (5) research to monitor patterns of treatment dissemination and quality of care through Patterns of Care/Quality of Care Studies, the Prostate Cancer Outcomes Study, and studies utilizing the SEER-Medicare Database. In addition, the NCI Community Cancer Centers Program (NCCCP) is researching how best to bring effective cancer treatments to patients in the communities where they live.

The population of cancer patients surviving more than 5 years continues to grow. NIH continues to support research and education aimed at professionals who deal with cancer patients and survivors. NIH cancer survivorship research addresses the physical, psychosocial, and economic impacts of cancer diagnosis and its treatment and the need for interventions to promote positive outcomes in survivors and their families. Important early findings suggest long latencies for treatment-related effects, highlighting the need for extended follow up, early identification, and intervention before complications become more serious.

To improve the outcomes of cancer patients, advances in knowledge must be effectively disseminated to the public and to health care providers. The Cancer Control P.L.A.N.E.T. Web portal is a collaborative effort aimed at providing access to data and resources that can help cancer control planners, health educators, program staff, and researchers design, implement, and evaluate evidence-based cancer control programs. P.L.A.N.E.T. assists local programs with resources that help them determine cancer risk and the cancer burden within their State and helps States identify potential partners. P.L.A.N.E.T. also provides online resources for interpreting research findings and recommendations and for accessing products and guidelines for planning and evaluation.

Infrastructure for Research

NIH places a high priority on technology development (see the section "Technology Development" in this chapter) to support both research and the application of research findings to improve health care delivery, emphasizing the areas of bioinformatics, cancer imaging, proteomics, and nanotechnology. As NIH-supported scientists begin to apply new discoveries to cancer prevention, early detection, and treatment, it will be increasingly important to integrate the tools and insights of research, science, and technology as effectively as possible.

The Cancer Biomedical Informatics Grid™ (caBIG™) is an important initiative that has been launched to accelerate research discoveries and improve patient outcomes by supporting the sharing of data and tools among researchers, physicians, and patients throughout the cancer community. NIH is committed to bringing caBIG™ into an enterprise model that can be extended and sustained across a broader community.

Another initiative, the NCI Alliance for Nanotechnology in Cancer, is a comprehensive endeavor that involves both the public and the private sectors and is designed to accelerate the application of the best capabilities of nanotechnology to cancer research. This initiative supports research on novel nanodevices to detect and pinpoint the location of cancer at its earliest stages, deliver anticancer drugs specifically to malignant cells, and determine in real time whether these drugs are effective in killing those cells.

Given the global burden of cancer and opportunities to identify new approaches in prevention and treatment through international collaborative research, NIH is strengthening health research infrastructure and building global research capacity through the International Tobacco and Health Research and Capacity Building Program. This program promotes transdisciplinary approaches to reduce the global burden of tobacco-related illness and is designed to promote international cooperation between U.S. investigators and scientists in low- and middle-income nations where tobacco consumption is a current or anticipated public health urgency. Because the overwhelming majority of smokers begin tobacco use before they reach adulthood, the program emphasizes research on determinants of youth smoking in diverse cultural and economic settings, as well as effective ways to prevent young people from starting to smoke.

Personalized Medicine

Advances in these critical aspects of cancer research are being synthesized into a vision of a future approach to health care called "personalized medicine," which will enable clinicians to use detailed molecular and clinical information about an individual's health to guide the selection of cancer therapies or preventive measures that are most likely to be safe and effective for that person. The NIH vision of personalized medicine spans the entire cancer continuum, from prevention through survivorship. Investments in risk assessment, treatment, and infrastructure development have already yielded progress toward reaching that vision. Potential benefits of personalized medicine include increased understanding of individual risk factors, earlier detection and more accurate diagnosis of cancer, more effective targeted treatment, increased likelihood of survival with improved quality of life, and implementation of high-quality, patient-centered cancer care through improved communication, informatics, and surveillance.

Notable Examples of NIH Activity

Key for Bulleted Items:

E = Supported through **E**xtramural research
I = Supported through **I**ntramural research
O = **O**ther (e.g., policy, planning, or communication)
COE = Supported through a congressionally mandated **C**enter **o**f **E**xcellence program
GPRA Goal = Concerns progress tracked under the **G**overnment **P**erformance and **R**esults **A**ct

Initiatives and Major Programs

Clinical Proteomic Technologies Initiative for Cancer: The completion of the Human Genome Project in 2003 has been a major catalyst for proteomics research, and NIH has taken a leading role in facilitating the translation of proteomics from research to clinical application through its Clinical Proteomic Technologies Initiative for Cancer. The overall objective of this Initiative is to build the foundation of technologies (assessment, optimization, and development), data, reagents and reference materials, computational analysis tools, and the infrastructure needed to systematically advance our understanding of protein biology in cancer and accelerate discovery research and clinical applications.

- For more information, see http://proteomics.cancer.gov
- This example also appears in Chapter 3: *Genomics* and Chapter 3: *Technology Development*.
- (E/I) (NCI)

NCI Alliance for Nanotechnology in Cancer: The NCI Alliance for Nanotechnology in Cancer is a comprehensive, systematized initiative that encompasses the public and private sectors and is designed to accelerate the application of the best capabilities of nanotechnology to cancer. The program supports research on novel nanodevices that may detect and pinpoint the location of cancer at its earliest stages, deliver anticancer drugs specifically to malignant cells, and determine in real time whether these drugs are effective in killing malignant cells. Nanotechnology is likely to change the very foundations of cancer diagnosis, treatment, and prevention.

- For more information, see http://nano.cancer.gov
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Technology Development*.
- (I/E) (NCI)

Cancer Imaging Program (CIP): The CIP's mission is to promote and support cancer-related basic, translational, and clinical research in the imaging sciences. CIP initiatives include (1) development and delivery of image-dependent interventions for cancer and pre-cancer; (2) development of standardized models for the design of clinical trials using imaging; (3) development of emerging imaging technologies, including nanotechnology, proteomics, and high-throughput screening; and (4) development of imaging methods to detect, treat, and monitor response to therapy.

- For more information, see http://imaging.cancer.gov
- This example also appears in Chapter 3: *Technology Development*
- (I/E) (NCI)

Clinical Trials Networks: The Clinical Trials Networks are part of the infrastructure that allows patients and community physicians access to national studies, facilitating the ability to put successful regimens into practice:

- The Community Clinical Oncology Program (CCOP) is a network for conducting cancer prevention and treatment clinical trials. In 23 years of CCOPs, more than 200,000 people have enrolled in treatment and prevention trials. An example is the Study of Tamoxifen and Raloxifene (STAR), which compares the effectiveness of these two drugs for reducing the incidence of breast cancer in postmenopausal women at increased risk of the disease. Initial results indicate that raloxifene is as effective as tamoxifen with fewer side effects. (For more information, visit http://www.cancer.gov/STAR and http://dcp.cancer.gov/programs-resources/programs/ccop.)
- Cooperative Group Trials consist of researchers, Cancer Centers, and community doctors who investigate new cancer treatment, prevention, early detection, quality of life, and rehabilitation. They involve more than 1,700 institutions, thousands of individual investigators, and more than 22,000 patients each year. These trials are testing therapies that demonstrate improvement to overall patient survival. For example, the Bevacizumab with Platin-Based Chemotherapy study showed that when the monoclonal antibody bevacizumab is added to a paclitaxel-carboplatin chemotherapy regimen for patients with NSCLC, their overall survival, progression-free survival, and response rates significantly increased. (For more information, visit http://ctep.cancer.gov.)
- The NCI Community Cancer Centers Program (NCCCP) is a 3-year pilot program to test the concept of a national network of community cancer centers to alleviate inadequate care delivery. NCCCP will develop and evaluate programs on community-based cancer care and identify ways to facilitate their broader engagement in cancer research. (For more information, visit http://ncccp.cancer.gov.)

    - This example also appears in Chapter 3: *Clinical and Translational Research*.
    - (E) (NCI)

Community Networks Program (CNP): The CNP aims to reduce and eliminate cancer disparities among racial minorities through community-based research, education, and training. The goals of the program are to significantly improve access to and utilization of beneficial cancer interventions in communities with cancer disparities. A total of 25 projects across the United States and in American Samoa were launched in May 2005 to address cancer disparities among African Americans, American Indians/Alaska Natives, Hawaiian Natives and other Pacific Islanders, Asians, Hispanics/Latinos, and rural underserved populations. Ten grantees work in local areas, 10 in regional areas, and 5 in national programs. Visit: http://crchd.cancer.gov/cnp/overview.html.

- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NCI)

Genome-Wide Association Studies of Cancer Risk: Beginning with the Cancer Genetic Markers of Susceptibility (CGEMS) initiative for breast and prostate cancer, NIH has capitalized on its long-term investment in intramural and extramural consortia by creating strategic partnerships to accelerate knowledge about the genetic and environmental components of cancer induction and progression. With powerful new technology capable of scanning the entire human genome, these efforts have recently identified unsuspected genetic variants associated with increased risk for developing cancers of the prostate, breast, and colon. Additional scans, either planned or under way, will be directed at cancers of the pancreas, bladder, lung, and other organs. The results of these genome-wide studies, together with the follow-on studies planned to narrow the search for causal gene variants, promise to provide novel clinical strategies for early detection, prevention, and therapy. To expand upon these emerging opportunities, a new Laboratory of Translational Genomics (LTG) has been established to further characterize genetic regions associated with cancer susceptibility and to identify gene-gene and gene-environment interactions. The LTG will create opportunities for collaboration and data sharing to accelerate the translation of genomic findings into clinical interventions.

- For more information, see http://cgems.cancer.gov/
- For more information, see http://epi.grants.cancer.gov/BPC3/cohorts.html
- For more information, see http://epi.grants.cancer.gov/PanScan
- For more information, see http://cgems.cancer.gov/index.asp
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies* and Chapter 3: *Genomics*.
- (E/I) (NCI)

NCI Experimental Therapeutics Program (NExT): The NExT program safely shortens the timeline for taking anticancer drugs from the laboratory to the clinic by combining NIH's expertise in drug development with state-of-the art research facilities. The program also utilizes new FDA guidelines that allow early Phase I clinical trials to proceed before certain time-consuming and expensive drug development steps occur. The first such study passed the initial stage of clinical examination demonstrating that this new type of trial can reduce the number of patients required for an early clinical study and the time necessary to gather critical drug development information.

- For more information, see http://dctd.cancer.gov/MajorInitiatives/02NExT.htm
- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (E/I) (NCI)

Systems Biology and Systems Genetics: NIH launched the Integrative Cancer Biology Program to focus on networks that can be measured, modeled, and manipulated rather than individual components. Multidisciplinary teams are critical to integrating the disciplines of biology, medicine, engineering, math, and computer science (e.g., computational biology). Equally important to our understanding of cancer is systems genetic research (systems biology and genetics). Networks of genes can be found and their associations tested and quantified with parallel association studies on relevant human populations.

- For more information, see http://icbp.nci.nih.gov
- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences* and Chapter 3: *Technology Development*.
- (E) (NCI)

The Cancer Biomedical Informatics Grid™: The Cancer Biomedical Informatics Grid™ (caBIG™) initiative has been launched to accelerate research discoveries and improve patient outcomes by linking researchers, physicians, and patients throughout the cancer community. date represents a new phase of evolution, as NIH is committed to bringing caBIG™ into an enterprise model that can be extended and sustained across a broader community.

- For more information, see http://cabig.cancer.gov
- This example also appears in Chapter 3: *Technology Development*.
- (E/I) (NCI)

The Cancer Genome Anatomy Project (CGAP): The goal of CGAP is to determine the gene expression profiles of normal, precancer, and cancer cells to improve detection, diagnosis, and treatment for the patient. The CGAP Web site makes various tools for genomic analysis available to researchers. Through worldwide collaborations, CGAP seeks to increase its scientific expertise and expand its databases for the benefit of all cancer researchers.

- For more information, see http://cgap.nci.nih.gov/
- This example also appears in Chapter 3: *Genomics*.
- (E/I) (NCI)

The Cancer Imaging Program (CIP): The mission of CIP is to promote and support cancer-related basic,

translational and clinical research in imaging sciences. CIP initiatives include: a) development and delivery of image-dependent interventions for cancer and pre-cancer; b) standardized models for the design of clinical trials using imaging; c) development of emerging imaging technologies, including nanotechnology, proteomics, and high-throughput screening; and d) development of imaging methods to detect, treat and monitor response to therapy.

- For more information, see http://imaging.cancer.gov/
- This example also appears in Chapter 3: *Technology Development*.
- (E/I) (NCI)

The NCI Alliance for Nanotechnology in Cancer: This is a comprehensive, systematized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. The program supports research on novel nanodevices that may detect and pinpoint the location of cancer at its earliest stages, deliver anticancer drugs specifically to malignant cells, and determine in real-time if these drugs are effective in killing malignant cells. Nanotechnology will likely change the very foundations of cancer diagnosis, treatment and prevention.

- For more information, see http://nano.cancer.gov/
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Technology Development*.
- (E/I) (NCI)

The Radiation Research Program (RRP): The RRP establishes priorities, allocates resources, and evaluates the effectiveness of radiation research and coordinates with other Federal radiation research programs. RRP has established guidelines for studying proton radiation therapy. Major trials are evaluating radiation dose escalation in NSCLC and novel combinations of chemotherapy with concomitant-boost radiation therapy in patients with NSCLC.

- Bonner JA, et al. *N Engl J Med*. 2006;354:567-78, PMID: 16467544
- Bao S, et al. *Nature*. 2006;444:756-60, PMID: 17051156
- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (I) (NCI)

The Tumor Biology and Metastasis Program: The Tumor Biology and Metastasis Program supports research to delineate the molecular mechanisms and signaling pathways involved in tumor progression, cell migration and invasion, angiogenesis, lymphangiogenesis, and metastasis. Research indicates that the progression of cancer depends on the co-evolution of carcinoma cells in their immediate microenvironment. In 2006, NIH launched the Tumor Microenvironment Network (TMEN) to investigate the composition of the stroma in normal tissues. The goal of this network is to delineate the mechanisms of tumor-stromal interactions in human cancer.

- For more information, see http://tmen.nci.nih.gov
- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NCI)

The NCI Vaccine Program: NCI's vaccine program develops novel vaccines for cancer immunotherapy and prevention and HIV. The program encourages collaborations, identifies organizational and reagent needs for the community, and develops the optimal infrastructure for vaccine development and novel clinical trial approaches. Gardasil®, the first vaccine to prevent cervical cancer induced by HPV, is now available and can potentially save more than 5,000 U.S. women's lives each year. This FDA-approved vaccine resulted from basic research performed at NIH that produced a prototype vaccine and the observation that linked HPV and cervical cancer.

- This example also appears in Chapter 2: *Infectious Diseases and Biodefense* and Chapter 3: *Clinical and Translational Research*.
- (E/I) (NCI)

Long-Term Cancer Survivors Research Initiatives: The population of cancer patients surviving more than 5 years continues to grow across life stages, from children through senior adults. These research initiatives focus on the physiological and psychosocial effects of treatment, as well as medical interventions to promote positive outcomes in survivors and their families. Important early findings suggest long latencies for treatment-related effects, highlighting the need for extended follow up, early identification, and intervention before complications become more serious. Implications include the length and quality of survival and the ongoing burden of illness and costs.

- For more information, see http://cancercontrol.cancer.gov/bb/2006_bb.pdf#page=93
- For more information, see http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-04-003.html
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NCI, CDC, NIA)

International Tobacco and Health Research and Capacity Building Program: Without a significant shift in worldwide smoking patterns, tobacco is projected to cause roughly 10 million deaths each year by 2025; 70 percent of this increase will occur in developing countries. To address this rising epidemic, NIH reissued the International Tobacco and Health Research and Capacity Building Program for funding in 2007. Grantees are generating a solid evidence base that can inform effective tobacco control strategies and policies. The program focuses on five critical areas: epidemiology and surveillance, susceptibility and risk for smoking uptake, behavioral and social sciences, effective interventions, and policy-related research. The program also emphasizes research on determinants of youth smoking in diverse cultural and economic settings. A central goal of this program is to strengthen capacity in tobacco research in low- and middle-income nations, which advances the science and permits greater international collaboration.

- For more information, see http://www.fic.nih.gov/programs/research_grants/tobacco/index.htm
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (FIC, NCI, NIDA, NIDCR, ORWH)

The Program in HIV/AIDS & Cancer Virology: The mission of the Program in HIV/AIDS & Cancer Virology is to facilitate and rapidly communicate advances in the discovery, development, and delivery of antiviral and immunologic approaches for the prevention and treatment of HIV infection, AIDS-related malignancies, and cancer-associated viral diseases. This includes basic laboratory, translational, and clinical studies of disease pathogenesis, the development of novel targeted treatment approaches for cancers in HIV-infected individuals and for HIV infection itself, and drug resistance. Recent advances include a new prophylactic vaccine for HPV and promising candidates for prophylactic and therapeutic vaccines against HIV infection.

- For more information, see http://ccr.nci.nih.gov
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*.
- (E/I) (NCI)

Trans-Institute Angiogenesis Research Program (TARP): TARP encourages and facilitates the study of angiogenesis, the formation of new blood vessels. A number of common disease conditions are angiogenesis dependent, including some cancers, macular degeneration, atherosclerosis, diabetic retinopathy, and many others. Cancers cannot grow beyond a certain size without new blood vessels. According to one estimate, more than 500

million people could benefit from anti- or pro-angiogenesis treatments in the coming decades. TARP funds promising angiogenesis research and provides training and workshops to communicate state-of-the-art preclinical and clinical angiogenesis research. The program's multidisciplinary approach fosters data exchange and resource sharing among vascular biology and angiogenesis researchers from different disease disciplines. A number of new angiogenesis inhibitors are currently being developed, including several in late-stage clinical trials.

- For more information, see http://www.tarp.nih.gov/funding.html
- (E) (**NCI**, NEI, NHLBI, NICHD, NIDDK, NINDS)

The Sister Study: The Sister Study is a major NIH initiative to study environmental and genetic risk factors for breast cancer in a cohort of 50,000 sisters of women who have had breast cancer. The asymptomatic women are being followed over time with periodic health updates. The women who develop breast cancer during the follow-up period will be compared with those who remained healthy to identify factors associated with increased cancer risk.

- For more information, see http://www.sisterstudy.org/English/index1.htm
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies*.
- (I) (NIEHS)

Brain Tumor: The NIH Brain Tumor Progress Review Group identified many priorities for the field. Research on understanding and preventing brain tumor dispersal was one of the group's highest scientific priorities, and NIH funds a number of projects in this area, many of which were submitted in response to a Program Announcement with set-aside funds issued in 2004. NIH also funds clinical studies investigating therapy delivery to the brain and evaluating the safety and tolerability of various therapies, including immunological therapies, vaccine therapy, monoclonal antibodies, and combination therapies. The Surgical and Molecular Neuro-Oncology Unit within the NIH Division of Intramural Research investigates basic mechanisms of brain tumor development and chemotherapy resistance to find new therapeutic strategies, particularly for malignant gliomas.

- For more information, see http://www.ninds.nih.gov/find_people/groups/brain_tumor_prg/index.htm
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E/I) (**NINDS**, NCI)

Cancer Stem Cells: NIH is expanding its research portfolio related to the basic biology of tumor-initiating cells (i.e., stem cells) within the hematological and solid-tumor malignancies. Tumor stem cells are a minor population of cells thought to be capable of reconstituting an entire tumor. This is extremely important clinically in that these cells may be responsible for the recurrence of malignancy. Progress has been made in identifying such minority populations of tumor stem cells in both multiple myeloma and acute myelogenous leukemia. These tumor-initiating cells are resistant to standard chemotherapeutic agents but may contain "stem cell-unique" target molecules that may allow their eradication with novel small molecular therapeutics. Progress in identifying tumor "stem cells" among solid tumors has also been made in breast cancer, where the minority of "stem cells" have been separated and characterized from the majority of breast cancer cells in the tumor.

- For more information, see http://stemcells.nih.gov/index.asp
- (E/I) (NCI)

Exemplary Current Studies and Projects

Cancer and Inflammation: NIH is actively pursuing research on the relationship between alterations in the lung microenvironment caused by inflammation and carcinogenesis. Inflammation is a response to acute tissue

damage, whether resulting from physical injury, ischemic injury, infection, exposure to toxins, or other types of trauma. Current research on inflammation suggests pro-inflammatory conditions such as chronic pulmonary irritation contribute to the development of lung cancer and may be strongly correlated with the occurrence of lung cancer in nonsmokers. Ongoing studies are investigating inflammation in stomach, liver, and other cancers.

- (E/I) (NCI)

Molecular Profiling of Cancer: The underlying cause of each patient's disease is typically unique to the individual. Because each tumor has its own biological properties, molecular profiling provides advanced analysis and tools to characterize each individuals' disease or tumor so that tailored medical strategies can be given. Several notable examples include:

- The Early Detection Research Network (EDRN) brings together dozens of institutions to help detect cancer in its earliest stages. EDRN was formed to bring a collaborative approach to the discovery, development, and validation of early detection markers by accelerating the translation of biomarker information into clinical applications.
- The Strategic Partnering to Evaluate Cancer Signatures (SPECS) Program establishes strategic partnerships to bring together interdisciplinary teams to evaluate the clinical utility of molecular signatures. SPECS focuses on confirming, evaluating, and refining signatures and/or profiles derived from molecular analysis of tumors (i.e., biomarkers detection) to improve patient management and outcomes.

- For more information, see http://edrn.nci.nih.gov/
- For more information, see http://www.cancerdiagnosis.nci.nih.gov/specs/index.htm
- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (E/I) (NCI)

The Cancer Genome Atlas (TCGA): TCGA is a comprehensive and coordinated effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. The goal of TCGA is to develop a free, rapidly available, publicly accessible, comprehensive catalog, or atlas, of the many genetic changes that occur in cancers, from chromosome rearrangements to DNA mutations to epigenetic changes–the chemical modifications of DNA that can turn genes on or off without altering the DNA sequence. The overarching goal of TCGA is to improve our ability to diagnose, treat, and prevent cancer.

- For more information, see http://cancergenome.nih.gov/index.asp
- This example also appears in Chapter 3: *Genomics* and Chapter 3: *Technology Development*.
- (E/I) (**NCI**, NHGRI)

Patient Navigation Research Program (PNRP): PNRP is an intervention that addresses barriers to quality standard care by providing individualized assistance to cancer patients and survivors and their families. The program's aim is to decrease the time between a cancer-related abnormal finding, definitive diagnosis, and delivery of quality standard cancer care. PNRP will focus on the four cancers with the greatest disparity in screening and follow-up care: breast, cervical, prostate, and colorectal cancers. Nine PNRPs reach African Americans, American Indians, Asians, Hispanics/Latinos, and rural underserved populations.

- For more information, see http://crchd.cancer.gov/pnp/pnrp-index.html
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NCI)

Advances in Oral Cancer Detection: The first product of a current NIH-funded research project to integrate new technologies into a reliable clinical protocol to improve oral cancer detection and survival has reached the market. Researchers report success using a customized optical device that allows dentists to visualize in a completely new way whether a patient might have a developing oral cancer. The simple, handheld device emits a cone of light into the mouth that excites molecules within our cells, causing them to absorb the light energy and re-emit it as visible fluorescence. When the light is removed, the fluorescence disappears. Changes in the natural fluorescence of healthy tissue can indicate light-scattering changes caused by developing tumor cells. Health care providers shine a light onto a suspicious sore in the mouth, look through an attached eyepiece, and check for changes in color. Normal oral tissue emits a pale green fluorescence, whereas early tumor cells appear dark green to black. The instrument is an effective screening adjunct and is useful for helping surgeons determine how far to extend the surgical borders when removing tissue for biopsies.

- For more information, see http://clincancerres.aacrjournals.org/cgi/content/full/12/22/6716
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Technology Development*.
- (E) (NIDCR)

Promoting Early Detection of Oral Cancer in African American Men: NIH is developing a new series of oral cancer education materials specifically for African American men, who have the highest risk of oral cancer and the lowest 5-year survival rate (only 35.6 percent) of any other population in the United States. This is the first national-level effort of its kind. The first piece in the series, "Are You at Risk for Oral Cancer? What African American Men Need to Know, is now being pre-tested in Washington, DC, Chicago, Los Angeles, and Columbia, South Carolina. The brochure–along with other complimentary education tools, such as fact sheets, posters, and both print and audio public service announcements–will be distributed to African American community groups around the country.

- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E/I) (**NIDCR**, NCI)

Research May Lead to Blood Test to Predict Cancer Treatment Response: In 2007, an estimated 34,000 Americans will be diagnosed with cancer of the oral cavity and pharynx (the middle part of the throat that includes the soft palate, tonsils, and tongue), and 7,550 Americans will die from it. Surgical treatment for these cancers may result in a loss of the ability to speak and swallow. In the largest long-term study of its kind, NIH-supported scientists determined that patients who showed a decline in specific cancer-related proteins after chemotherapy and radiation are more likely to remain in remission. These patients may not need to undergo surgery that may rob them of their speech and swallowing abilities. These findings could help lead to the development of a blood test that enables doctors to detect the recurrence of throat cancer at an early stage. A blood test that enables doctors to closely monitor a patient's rehabilitation while sparing the patient's voice, speech, and swallowing ability is an excellent example of NIH's predictive, preemptive, and personalized approach to medicine.

- Allen C, et al. *Clin Cancer Res* 2007;13:3182-90, PMID: 17545521
- (I) (NIDCD, NCI)

The Dog Genome and Human Cancer: Cancer is the number-one killer of dogs, and studying the major cancers in dogs provides a remarkably valuable approach for developing a better understanding of the development of cancer in humans. The clinical presentation, histology, and biology of many canine cancers very closely parallel those of human malignancies, so comparative studies of canine and human cancer genetics should be of significant clinical benefit to both species. Furthermore, information gained from studying the genetic variant involved in dog size can provide important information for studying cell growth in humans and has the potential to be a useful tool

in cancer research. A 2007 article by NIH's Dr. Elaine Ostrander and colleagues reported a genetic variant that is a major contributor to small size in dogs. In the following month, Dr. Ostrander and colleagues published a study reporting that a mutation in a gene that codes for a muscle protein can increase muscle mass and enhance racing performance in dogs.

- Sutter NB, et al. *Science* 2007;316:112-5, PMID: 17412960
- Mosher DS, et al. *PLoS Genet* 2007;3:e79, PMID: 17530926
- For more information, see http://www.genome.gov/25520294
- This example also appears in Chapter 3: *Genomics* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (I) (NHGRI)

Salivary Gene Transfer and Therapeutics: Gene transfer may be an ideal strategy to boost salivary production for cancer patients whose salivary glands were damaged during radiation therapy. Although radiation therapy kills cancerous cells, it frequently also destroys the acinar (fluid-producing) salivary gland cells that lie within the salivary gland in grapelike clusters. Patients are unable to produce adequate saliva and suffer a host of long-term problems such as recurrent oral infections and difficulties with swallowing, speech, and taste. Unlike acinar cells, ductal cells in the salivary gland (which can be thought of as the "stems" on the grapes) often survive irradiation. However, they cannot make or secrete saliva. NIH scientists used gene transfer techniques to insert an aquaporin protein gene into the ductal cells; aquaporins are a family of proteins that form pores in cell membranes, through which fluid can pass. Their insertion "plumps up" the stems and allows the flow of fluid into the mouth again. The scientific team has collaboratively and methodically moved this promising idea through the research process, benefiting greatly from the wealth of scientific expertise on the NIH campus. This year, FDA approved the first clinical trial of gene transfer into the salivary glands for cancer patients with dry mouth. Although the outcome of clinical trials is always hard to predict, the preclinical data have been extremely promising.

- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (I) (NIDCR)

Cancer.gov in Español: This Spanish-language version of the NCI Web site is designed to reach the Hispanic-Latino population–the fastest growing online audience in the country–to communicate the message that cancer can be prevented and treated and to offer information on all aspects of the disease. The site is specifically tailored for Hispanics and Latinos, and pages are organized around issues of greatest concern. The site will be updated with evidence-based approaches and emerging technologies to ensure that accurate, relevant, and audience-appropriate information is provided. The site demonstrates the commitment to reducing cancer health disparities by making information readily available to underserved populations.

- For more information, see http://www.cancer.gov/espanol
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E) (NCI)

Accomplishments

A Multidisciplinary Approach to Nicotine Addiction: Nicotine addiction is the number-one preventable public health threat and has enormous associated morbidity, mortality, and economic costs. NIH-supported research has generated new knowledge to support the development of more effective prevention messages and treatment approaches. Several notable examples characterize NIH's multidisciplinary approach to targeting the best treatment (or combination of treatments) for nicotine addiction. Genomic studies have recently uncovered a series of genes that are associated with nicotine addiction and that could provide new targets for medication

development and for the optimization of treatment selection. Pharmacologic studies, critical to understanding the basis of nicotine's mode of action, have recently revealed that its addictiveness may hinge upon its ability to slowly shut down or desensitize the brain's response to nicotine. A recent imaging study indicated that a part of the brain called the insula may play an important role in regulating conscious craving. This exciting finding provides a new target for research into the neurobiology of drug craving and for the development of potentially more effective smoking cessation and other addiction treatments. Results of a Phase II clinical trial strongly suggest that a nicotine vaccine, which works by preventing nicotine from reaching the brain, may be a particularly useful tool for cessation programs in the not-too-distant future.

- For more information, see http://www.drugabuse.gov/researchreports/nicotine/nicotine.html
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*, Chapter 3: *Clinical and Translational Research*, and Chapter 3: *Genomics*.
- (E) (**NIDA**, NCI) (GPRA Goal)

Developmental Windows of Vulnerability to Environmental Exposures: The Breast Cancer and Environment Research Centers (BCERCs) supported by NIH function as a consortium to study the impact of prenatal to adult environmental exposures that may predispose a woman to breast cancer. The centers bring together basic scientists, epidemiologists, research translational units, and community advocates within and across the centers to investigate mammary gland development in animals and young girls to determine vulnerability to environmental agents that may influence breast cancer development in adulthood. The overall goals of the BCERC are to develop public health messages to educate young girls and women who are at high risk of breast cancer about the role of specific environmental stressors in breast cancer and how to reduce exposures to those stressors. These public health messages will be based on the integration of basic biological, toxicological, and epidemiological data.

- For more information, see http://www.bcerc.org
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (**NIEHS**, NCI) (GPRA Goal)

Clinical Trials Education: The materials in the Clinical Trials Education series represent a collection of over 20 resources developed to increase awareness and participation in cancer prevention and treatment clinical trials. These materials include workbooks, a guide for community outreach, a trainer's guide, online courses for health professionals, DVDs, and slide sets to assist in education programs.

- For more information, see http://www.cancer.gov/clinicaltrials/learning/clinical-trials-education-series
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E/I) (NCI)

Health Care Delivery Consortia to Facilitate Discovery and Improve Quality of Cancer Care: NIH supports several research consortia that are designed to enhance understanding of cancer control across the continuum of prevention, screening, and treatment within the context of health care delivery.

- The most comprehensive of these initiatives, the Cancer Research Network (CRN), seeks to improve the effectiveness of preventive, curative, and supportive interventions for major and rare tumors. The CRN consists of the research programs, enrolled populations, and data systems of 13 health maintenance organizations covering care for more than 9 million enrollees, or 3 percent of the U.S. population. This initiative uses a consortium of delivery systems to conduct research on cancer prevention, early detection, treatment, long-term care, and surveillance. Given its large and diverse populations, the CRN is uniquely

positioned to study the quality of cancer care in community-based settings and to explore rare conditions. Seminal research includes CRN research documenting specific gaps in implementing effective tobacco cessation services among clinicians, reasons for late diagnosis of breast and cervical cancers, more rapid uptake in the use of aromatase inhibitors in comparison with tamoxifen in treatment for breast cancer, and examination of the role of a number of common drugs and cancer outcomes using its large and automated pharmaceutical databases.

- In the area of the evaluation of cancer screening in clinical care, the Breast Cancer Surveillance Consortium (BCSC) is a collaborative network of mammography registries linked to tumor and/or pathology registries. The network is designed to assess the delivery and quality of breast cancer screening and related patient outcomes in the United States. Because of the vast size and continually updated clinical information in this research initiative, the BCSC is responsible for research that, for the first time, documented the falling incidence of hormone replacement therapy among screened women; quantified the extent of difference in the association of breast density with breast cancer risk among pre- and postmenopausal women; and determined that, although biopsy rates are twice as high in the United States than in the United Kingdom, cancer detection rates are very similar in the two countries.
- The Cancer Care and Outcomes Research Surveillance Consortium (CanCORS) was established to identify how characteristics of patients, providers, and care delivery systems affect the cancer management and treatment services that patients receive, as well as the relationship between cancer-related clinical practices and outcomes, including patient-centered outcomes such as symptom control and quality of life. CanCORS supports prospective cohort studies on 10,000 patients with newly diagnosed lung or colorectal cancers across geographically diverse populations and health care systems and examines issues related to health outcomes, costs, and patient-centered issues such as symptom control and quality of life.

    - For more information, see http://crn.cancer.gov
    - For more information, see http://breastscreening.cancer.gov
    - For more information, see http://healthservices.cancer.gov/cancors
    - This example also appears in Chapter 3: *Clinical and Translational Research*, Chapter 3: *Epidemiological and Longitudinal Studies*, and Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
    - (I) (NCI)

Childhood Cancer Survivors Study (CCSS): Although survival rates from childhood cancers are encouraging, researchers have found that these young survivors may particularly suffer from late effects of treatment. In 2006, CCSS researchers documented serious long-term health issues in adults after radiation for childhood cancers. These findings will change treatment regimen guidelines for current childhood cancers and have implications for individuals from the study who are now adults. The Children's Oncology Group (COG) has prepared a resource for physicians, Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers.

- For more information, see http://www.cancer.gov/cancertopics/coping/childhood-cancer-survivor-study
- For more information, see http://www.survivorshipguidelines.org
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NCI)

The Centers for Transdisciplinary Research on Energetics and Cancer (TREC): These Centers foster collaboration among transdisciplinary teams of scientists to accelerate progress toward reducing cancer incidence, morbidity, and mortality associated with obesity, low physical activity, and poor diet. The biology and genetics of the many factors that influence diet, physical activity, and obesity across the stages of life are applied to behavioral, sociocultural, and environmental factors, and transdisciplinary training opportunities are provided for scientists. The TREC initiative is interfacing with a number of established NCI initiatives in the area of diet, physical activity,

and weight and is integrated with the NIH Obesity Research Task Force Strategic Plan.

- For more information, see http://cancercontrol.cancer.gov/trec
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NCI)

Transdisciplinary Tobacco Use Research Centers: Multiple Institutes at NIH are co-funding seven collaborative, transdisciplinary centers to identify familial, early childhood, and lifetime psychosocial pathways related to smoking initiation, use, cessation, and patterns of dependence. Research on genetics of addiction, physiological biomarkers, and the use of advanced imaging techniques can lead to individualized and community approaches for tobacco prevention and treatment. This model demonstrates the feasibility and benefits of scientific collaboration across disciplines and public-private partnerships.

- For more information, see http://dccps.nci.nih.gov/tcrb/tturc
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (**NCI**, NIAAA, NIDA)

Reports of the Clinical Trials Working Group (CTWG) and the Translational Research Working Group (TRWG): Recognizing the importance of translational and clinical research, two recently released, major reports of comprehensive evaluations will lead to more rapid progress in translating important research findings into new, effective interventions. The CTWG and TRWG were constituted as broad and inclusive panels (memberships comprise experts from academia, the pharmaceutical industry, advocacy groups, NIH, and other governmental agencies) to review and evaluate the current portfolio of research in this area and to identify ways to synergize, integrate, and coordinate efforts.

- For more information, see http://www.cancer.gov/trwg
- For more information, see http://integratedtrials.nci.nih.gov.
- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (E/I) (NCI)

Patient and Health Professional Education and Outreach: NIH provides comprehensive cancer information to those at risk and to patients, caregivers, and health care providers. This information ranges from prevention, through treatment, to end-of-life topics. For example, clinical sites across the country extensively utilize NIH print and Web-based materials to support their educational programs. The Cancer Information Service (CIS) effectively communicates information through a Partnership Program to help reach those with limited access to health information; an Information Service that provides cancer information by telephone, TTY, instant messaging, and e-mail; and a Research Program that helps advance health communication practices.

- For more information, see http://www.cancer.gov (click on "NCI Publications")
- For more information, see http://www.cancer.gov/cancertopics
- For more information, see http://www.cancer.gov/aboutnci/epeco
- For more information, see http://cis.nci.nih.gov
- This example also appears in Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E/I) (NCI)

Surveillance, Epidemiology, and End Results (SEER) Program and Software Analysis Tools: SEER is an authoritative source of information on cancer incidence and survival in the United States. Publications such as the Annual Report to the Nation on the Status of Cancer, as well as interpretation of recent trends in cancer, inform the public,

researchers, Federal and private agencies, and Congress on national cancer rates and trends. SEER is the only comprehensive source of U.S. population-based information that includes stage of cancer at the time of diagnosis, patient survival, and treatment. Linkage with Medicare and other Federal databases yields information sources that are used routinely to answer major questions on quality, cost, and variability of cancer care, as well as differences by racial and ethnic populations. SEER currently collects and publishes data from approximately 26 percent of the U.S. population. The team is developing computer applications to unify cancer registration systems, analyze and disseminate data, and provide limited access to the public file. SEER is considered the standard for quality among cancer registries around the world.

- For more information, see http://seer.cancer.gov/
- For more information, see http://surveillance.cancer.gov/
- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
- (E) (NCI)

Cancer Control P.L.A.N.E.T.: The Cancer Control P.L.A.N.E.T. (Plan, Link, Act, Network with Evidence-Based Tools) Web portal is a collaboration aimed at providing access to data and resources that can help cancer control planners, health educators, program staff, and researchers design, implement, and evaluate evidence-based cancer control programs. It assists local programs with resources that help them determine cancer risk and cancer burden within their State. It also helps States identify potential partners and provides online resources for interpreting research findings and recommendations and accessing products and guidelines for planning and evaluation.

- For more information, see http://cancercontrolplanet.cancer.gov
- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
- (E) (NCI)

The Minority Institution/Cancer Center Partnership (MI/CCP): The MI/CCP provides support for Minority-Serving Institutions (MSI) to partner with Cancer Centers. MI/CCP goals include: (1) increasing the participation of MSIs in the Nation's cancer research and training enterprise, (2) enhancing the number of competitive grant funding from minority investigators, (3) augmenting the research capacity at MSIs, (4) increasing the involvement and effectiveness of the Cancer Centers in research and training relating to ethnic minorities, and (5) developing more effective research, outreach, and education programs that will have an impact on ethnic minority and underserved populations.

- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NCI)

Transdisciplinary Tobacco Use Research Centers: Multiple Institutes at NIH are co-funding seven collaborative, transdisciplinary centers to identify familial, early childhood, and lifetime psychosocial pathways related to smoking initiation, use, cessation, and patterns of dependence. Research on genetics of addiction, physiological biomarkers, and the use of advanced imaging techniques can lead to individualized and community approaches for tobacco prevention and treatment. This model demonstrates the feasibility and benefits of scientific collaboration across disciplines and public-private partnerships.

- For more information, see http://dccps.nci.nih.gov/tcrb/tturc
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (**NCI**, NIAAA, NIDA)

Databases for Cervical Cancer Research: NIH has developed data analysis and image recognition tools for studying biomedical images of HPV infection and cervical neoplasia. Image data include 100,000 cervicographs (high-definition cervical photographs), Pap test, and histology images. Tools allow the exploration of visual aspects of HPV and cervical cancer for research, training, and teaching.

- Castle PE, et al. *Cancer Res* 2006;66:1218-24, PMID: 16424061
- Jeronimo J, et al. J *Low Genit Tract Dis* 2006;10:39-44, PMID: 16378030
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies* and Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
- (I) (**NLM**, NCI)

Understanding the Interface Between Aging and Cancer: Through a collaborative effort between NIA and NCI, eight NCI-designated Cancer Centers are developing studies on the biology of aging and cancer; patterns of care, treatment efficacy, and tolerance; the effects of comorbidity, prevention, and screening in older persons; and symptom management and palliative care in older patients. This research will help gain insights into why cancer occurs more frequently in older people, whether cancer behaves differently in older adults than in younger people, and how we need to adapt prevention and screening services to reach a greater number of older people as well as to aid in the development of predictive models for tolerance to therapy.

- For more information, see http://www.nci.nih.gov/newscenter/pressreleases/AgingGrants
- (E) (**NCI**, NIA)

NIH Strategic Plans Pertaining to Cancer

National Cancer Institute (NCI)

- *NCI Strategic Plan for Leading the Nation*
- *The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2007*
- *The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2008*

National Institute of Dental and Craniofacial Research (NIDCR)

- *NIDCR Strategic Plan*
- *NIDCR Implementation Plan*

National Center for Complementary and Alternative Medicine (NCCAM)

- *Expanding Horizons of Health Care: Strategic Plan 2005-2009*

John E. Fogarty International Center (FIC)

- *Pathways to Global Health Research* (Draft)

Office of AIDS Research (OAR)

- *FY 2008 Trans-NIH Plan for HIV-Related Research*

Other Trans-NIH Plans

- *Report of the Brain Tumor Progress Review Group*
  (NCI, NINDS)