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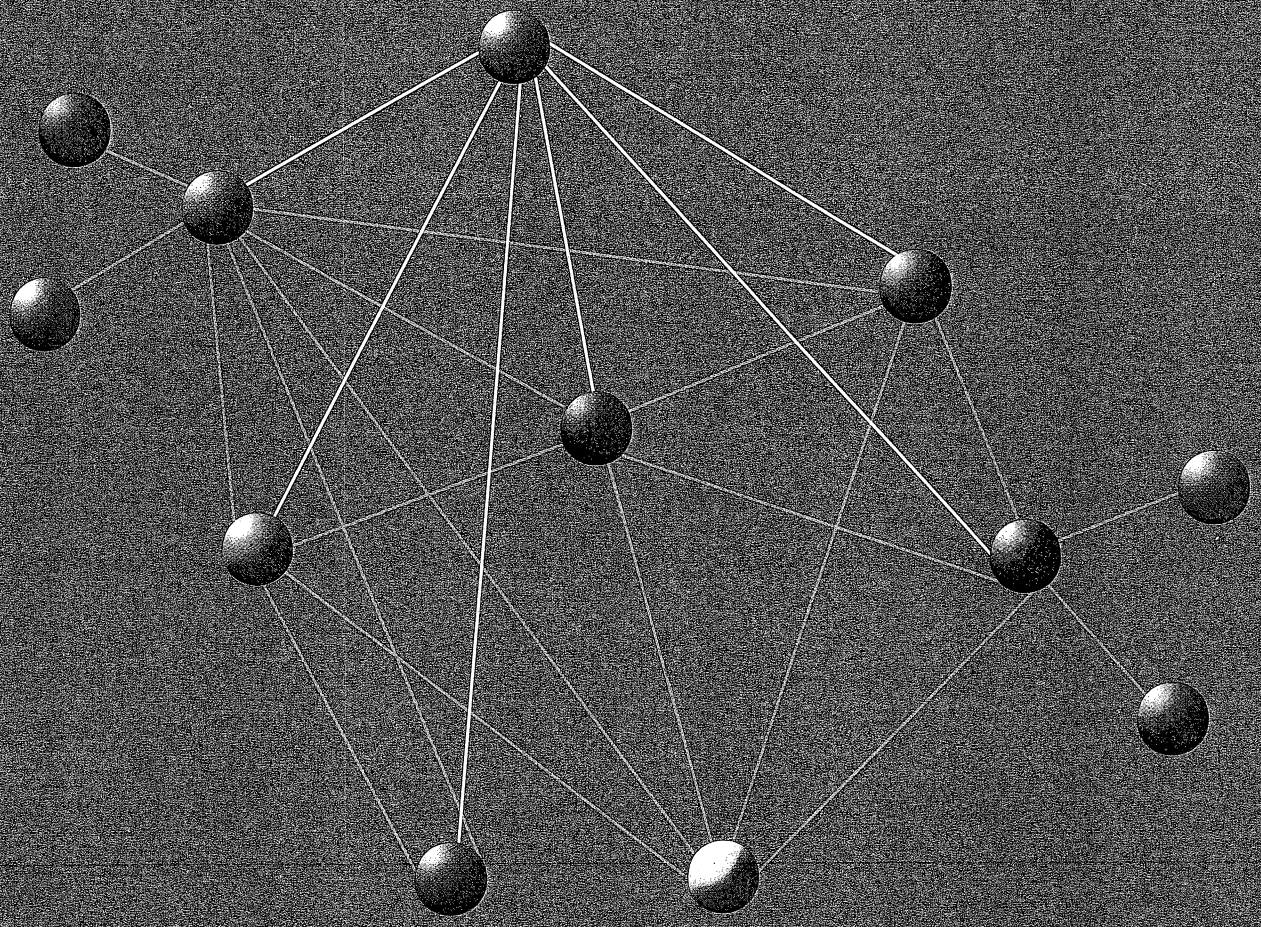
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NATIc

National Advanced Technology Initiative for Cancer

Eliminating the Suffering and Death DUE TO CANCER

Challenge goal 2015 – an overview

One American dies every minute as a result of cancer. Despite this grim statistic, it is clear that our medical and scientific communities are making tremendous progress. Three decades ago, there were 3 million cancer survivors in the United States; today, there are nearly 10 million. Death rates from the four most common cancers—lung, breast, prostate, and colorectal—continue to decline, indicating that our nation's investment in cancer research is paying dividends. The most significant benefit of that commitment, however, is about to be realized.

Over the past three decades, our struggle to cure cancer in the patient has been paralleled by our quest to understand cancer in the laboratory. Now we are poised to capitalize on the outputs of that *Discovery* process and *Develop* more effective interventions that, when *Delivered* to patients, will preempt the cancer process and eliminate a fatal outcome. Indeed, we are poised to eliminate the suffering and death due to cancer, and the NCI has committed to making this goal possible for all Americans by the year 2015.

This is a bold and visionary challenge. But it is one befitting the greatness of America. It is based on a rationale firmly rooted in the explosive pace of progress spawned by our robust biomedical research enterprise—an enterprise in which cancer researchers have consistently been at the forefront. NCI has led the effort over the past three decades to put into place the research and clinical programs required to effectively fight this disease. During this time, a national network of cancer centers has been established; an unsurpassed and robust basic and clinical research enterprise has been developed; and the cancer community has amassed a remarkable understanding of the mechanisms by which cancer develops and eventually progresses to its lethal state.

As a result of our continued commitment and understanding, we are now poised to exploit new opportunities to prevent many more cases of cancer; detect cancer at its earliest state; and, once cancer has been diagnosed, attack the disease at its weakest points and either eliminate it completely or keep it in check, much as we do with many chronic diseases. We will also maintain our commitment to applying research findings in the area of cancer control and population sciences to elucidate the role that behavioral, lifestyle, genetic, and environmental factors play in cancer initiation and progression.

To succeed, we must continue to drive the engine of discovery, fueled by fundamental research. Although our knowledge of cancer has expanded tremendously, we must learn more. So we have renewed our commitment to making new discoveries about cancer's genetic, molecular, and cellular puzzle. These discoveries are being translated into the development of new interventions—interventions that are designed for detection, diagnosis, and prediction, as well as treatment and prevention. Finally, once we develop these interventions, we will do what is necessary to ensure that they reach all who are in need.

Today, NCI continues to use the resources available to us as wisely and efficiently as possible. We have provided the leadership that has made the 2015 goal achievable, and we are defining the strategies necessary to achieve it and directing the tactics to make it a reality. Below are just a few of the initiatives and strategies that we believe are critical to meeting the 2015 goal.

Initiatives that take advantage of advanced technology…

- ***The Cancer Biomarker Project*** is identifying protein patterns and other molecular changes in saliva, sera, urine, or biopsy tissue that indicate the presence of a precancerous lesion or malignant tumor.
- ***The Advanced Cancer Imaging Project*** is moving us beyond anatomical to "next-phase" imaging methods that can more effectively detect and monitor cancer inside the body.
- ***The Cancer Nanotechnology Project*** will add a battery of agents and devices that function at the atomic and molecular levels, allowing for real-time monitoring of genetic and other changes associated with cancer.
- ***The Cancer Genome Project*** will allow researchers to systematically characterize the genes involved in nearly all forms of cancer.
- ***The Cancer Biomedical Informatics Grid*** will provide the critical informatics infrastructure that, for the first time ever, will connect teams of cancer and biomedical researchers from across the country, enabling them to share cutting-edge tools and data and vastly enhancing their ability to make rapid discoveries.

… Are leading to more effective cancer prevention, detection, control, and treatment strategies:

- ***Early Detection of Cancer*** – Novel approaches are being developed to prevent or intervene in the process of cancer development as well as more effectively treat the disease.
- ***Molecular Diagnosis*** – Clinicians will move beyond simply reacting to patient symptoms, instead performing molecular profiling and detection aimed at preempting cancer at the earliest possible stages.
- ***Molecularly Targeted Therapies*** – We are identifying genes and p roteins that contribute to cancer development and progression and translating these discoveries into validated "targets" for new therapies.
- ***Combination Therapies*** – We are moving toward strategically combining chemotherapeutic agents, radiation therapy, targeted molecular interventions, biologic response modifiers, and immunotherapy to more effectively treat patients, including tailoring such combinations to meet individual patients' needs.
- ***Prevention*** – The ultimate success in fighting cancer will be vast improvements in prevention, relying on new knowledge and tools to halt cancer from ever taking root or from progressing to a lethal form.

The 2015 challenge goal is not a prediction of what might be done; rather, it is an urgent call to do all that can be done. It will require a concerted, collaborative effort by the entire community. It will also require the simple belief—based on our ever-expanding wealth of knowledge and reliance on advanced technology—that eliminating the suffering and death due to cancer is, in fact, achievable. At the NCI, we believe that the goal is within our grasp, and we are prepared to stretch the boundaries of science, imagination, and human will to achieve success.

Andrew C. von Eschenbach, M.D.
Director,
National Cancer Institute

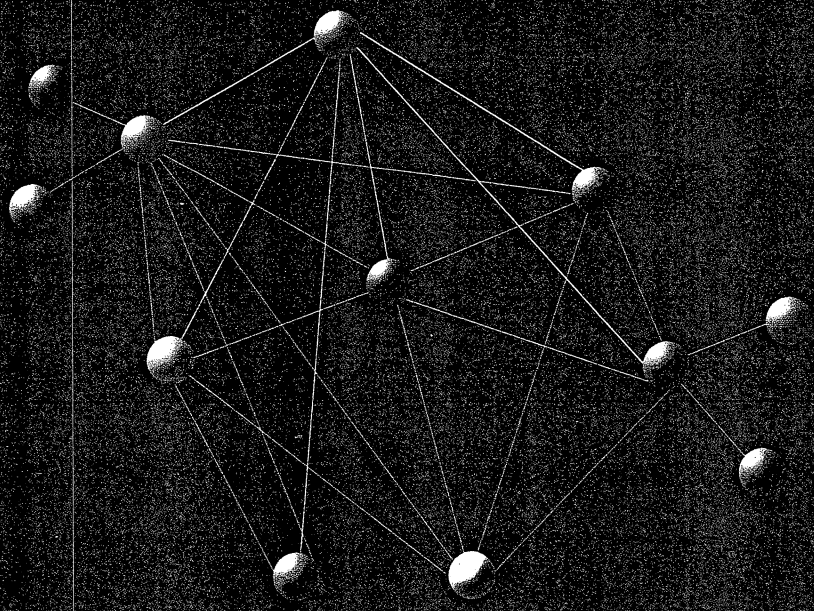


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National Advanced Technology Initiative for Canc

National Cancer Institute

NATIONAL ADVANCED TECHNOLOGY INITIATIVE FOR CANCER

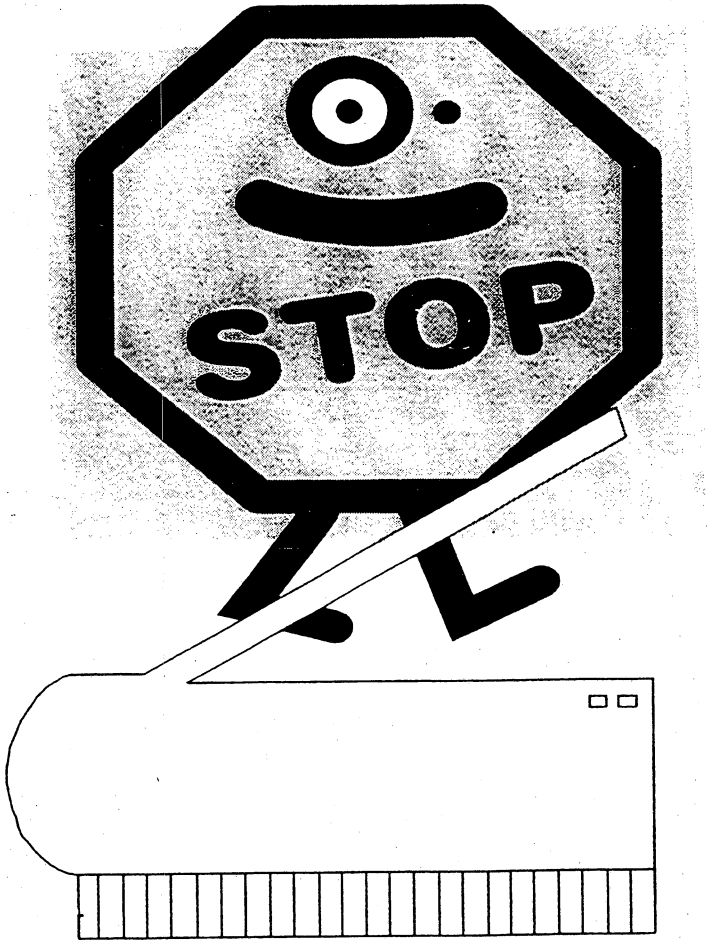


Business Plan

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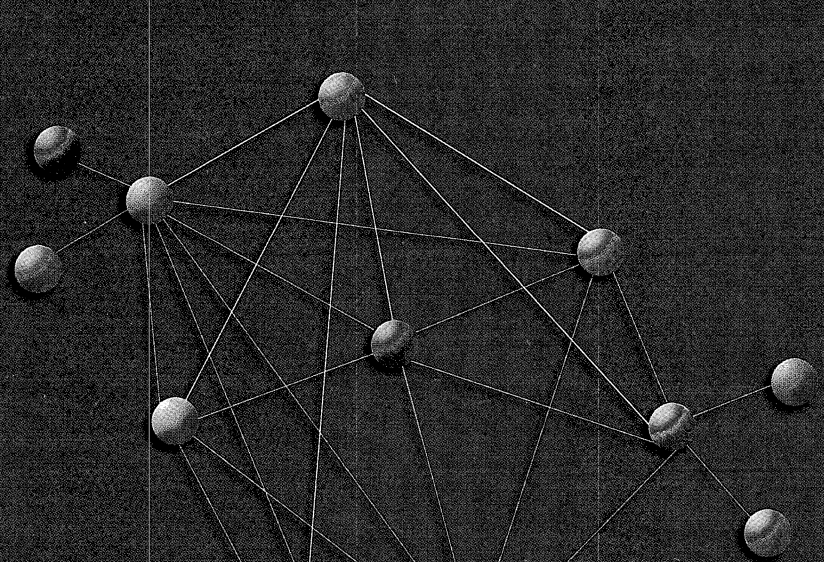
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Business Plan

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Business Plan for the National Advanced Technology Initiative for Cancer (NATIc)

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Executive Summary

The National Cancer Institute will establish an unprecedented national advanced technology development network, supported through the combination of a designated congressional appropriation, NCI operating funds, and philanthropy, to create the revolutionary diagnostics, preventives, and therapies needed to secure the conquest of cancer and other diseases in the next decade.

The human and economic burden of cancer for our Nation is enormous. More than 1.4 million Americans will receive a diagnosis of cancer in 2004, and at current rates, one in two men and one in three women will receive similar sobering news in their lifetime. Although death rates for certain cancers are declining and 5-year survival for many cancers is increasing, 560,000 people will die of cancer this year and the cost of the disease will exceed $180 billion. As baby boomers age, the number of new cancer cases will further increase the burden. To counter these daunting statistics now, the *National Cancer Institute (NCI) has set a goal for the Nation:* ***to eliminate the suffering and death due to cancer by the year 2015****. To secure this victory, the NCI is proposing the establishment of the National Advanced Technology Initiative for Cancer (NATIc).*

The NATIc will create and coordinate an unprecedented array of nationwide advanced health care technology development resources and complement and leverage the National Institutes of Health (NIH) Roadmap initiatives. Through formal clusters of institutions, or "hubs," consisting of the Nation's Cancer Centers, State and regional technology development consortia, national laboratories, and the Department of Health and Human Services (DHHS) Federally Funded Research and Development Center (FFRDC) at Frederick, Maryland, the NCI will optimize and accelerate the transfer, development, and commercialization of advanced health care technologies.

The NATIc will usher in a new era in cancer research (and indeed biomedicine) that cannot be achieved within the context of the NCI's current operating budget. Building on discoveries from basic and clinical research, this complementary initiative will allow the United States to create a robust infrastructure for the development of a new generation of advanced diagnostics and therapies for cancer and other diseases. To ensure that the advanced cancer technologies that derive from the NATIc reach patients at the earliest possible time, the "hubs" that comprise this "network of networks" will foster innovation and entrepreneurship and place significant emphasis on novel partnerships with the private and philanthropic sectors. The NCI has initiated efforts to develop intellectual property strategies that will ensure the public availability of the technologies developed through the NATIc while preserving incentives for commercialization.

The NATIc will comprise a nationwide network of approximately 10 virtually integrated advanced technology hubs and a small number of specialized technology "nodes." A central technical coordinating hub and management structure will be established to provide key core services and to optimize the performance of the overall NATIc for achieving key milestones. Funding for the NATIc will come from three sources: a NATIc annual Federal appropriation of $300 million per year for five years; $500 million from NCI's operations and a commitment to continue an appropriate level of funding after the NATIc Federal appropriation is outlayed; and $500 million from philanthropy.

It is projected that the advanced technologies that come from the NATIc will produce breakthroughs such as a catalogue of every genetic abnormality for all cancers, a comprehensive set of biomarkers to define the type and stage of most cancers, a targeted drug development system that will deliver over 20 new targeted drugs per year, and revolutionary nanotechnology-based cancer diagnostics. This new generation of advanced biomedical technologies will accelerate the realization of the NCI's goal to eliminate the suffering and death due to cancer, enable the realization of personalized medicine for all Americans, fuel the biotechnology industry, and increase U.S. competitiveness. Overall, the NATIc will be a beacon of hope for patients that cancer can be conquered and it is a critical and required strategic element for delivering on that hope.

This Business Plan provides a brief background, rationale, and projected management plan for the NATIc. It defines the overall strategy for securing the Federal appropriation, obligation schedule, outlay rates, and anticipated cash flow. It also provides an analysis of funding mechanisms and additional authorities that may be needed to accomplish the goals of the NATIc. Finally, it presents a summary of the milestones and deliverables that can be expected from the NATIc.

Chapter 1: Background and Rationale

An explosion of scientific knowledge of the processes leading to cancer coupled with the rapid emergence of advanced technologies (such as genomics, bioinformatics, proteomics, and nanotechnology) have created an unimagined opportunity to achieve exponential progress against cancer. The National Cancer Institute (NCI) has challenged America to act now and turn today's promise into unprecedented future progress—**to eliminate the suffering and death due to cancer by 2015**. To this end, the NCI proposes that we take a bold and pivotal step toward realizing this goal through the launch of the **National Advanced Technology Initiative for Cancer (NATIc)**. The NATIc will complement and leverage the National Institutes of Health (NIH) Roadmap initiatives and capitalize on State and regional investments in advanced technology development. Although the NATIc will be cancer led, the advanced health care technologies that emanate from it will ultimately accelerate the realization of personalized medicine to improve the health of all Americans.

The Cancer Burden: NCI has issued this challenge to the Nation because each minute of every hour of every day, one person dies from cancer. At current rates, cancer will become an even greater U.S. health care burden in the next 10-20 years due primarily to the aging of the U.S. population, especially the 76 million "baby-boomers." One in two men and one in three women in the United States now receives a cancer diagnosis, and more than half a million Americans will die from this disease in 2004. Health care costs attributable to cancer exceed $180 billion per year, primarily due to lost productivity from premature deaths. In fact, researchers recently estimated that reducing the cancer death rate by as little as 20 percent would add an estimated $10 trillion to the U.S. economy.[1]

These are daunting statistics, but advances in biomedical research, exemplified by the sequencing of the human genome, offer realistic promise that cancer can be prevented, cured, or managed successfully as a chronic disease. Realizing this vision will require that we move from our current state of a fragmented cancer research enterprise to a new system. The NATIc is a bold new concept in biomedicine that will harness the Nation's biomedical technology resources and capabilities through a virtually integrated network of advanced technology development hubs. The NATIc will complement and capitalize on discoveries from basic research and provide the Nation with a badly needed capability to efficiently and effectively translate important scientific discoveries into the 21st century technologies that will significantly accelerate the conquest of cancer and other diseases.

Improving Survival Statistics: When the war on cancer began in 1971 with the passage of the National Cancer Act, there were 3 million U.S. cancer survivors. Today there are in excess of 10 million. This more than tripling of the number of Americans surviving cancer reflects the steady decreases in death rates from the most common cancers and a 5-year survival rate of over 60 percent for all cancers. These statistics mirror our increased understanding of cancer as a disease process that provides new opportunities to develop new diagnostics and targeted interventions for both therapy and prevention.

NCI's Cancer Research Resource Base: These improving survival statistics reflect in part the unparalleled cancer research resource base that has evolved since the signing of the National Cancer Act in 1971. The NCI's budget in FY 2004 is approximately $4.7 billion, which supports more than 5,000 highly skilled investigators, most of whom reside at the institutions that also house the Nation's 61 Cancer Centers and 60 Specialized Programs of Research Excellence (SPOREs). The SPOREs represent teams of scientists who focus on studying a specific type of cancer such as breast, prostate, or lung. Many of the NCI's Cancer Centers work in partnerships with more than 650 academic health centers and 10,000 physicians to provide a national cancer research and care structure. More than 200,000 patients per year participate in clinical trials evaluating new potentially more effective cancer therapies. The current NCI-supported portion of the cancer research enterprise represents a significant return on

[1] Murphy, K, and R. Topel. The Value of Medical Research. University of Chicago Press, 2002

investment for the Nation in terms of both its impact on the diagnosis and treatment of cancer and its key role in fueling the biomedical revolution of the past decade.

Catalyzing a New Era: Advances in biomedical research over the past 30 years, especially during the past 5 years in which funding levels for the National Institutes of Health doubled, have produced an ever-clearer picture of how normal cells become cancerous and spread through the body. This discipline-focused research has already produced significant changes in the technologies available to diagnose cancer through advances in imaging and the discovery of targeted drugs such as Gleevec® and Herceptin®. These are outstanding examples of the convergence of discoveries from individual investigators addressing fundamental biological questions with the technology development capabilities needed to convert them into new molecularly targeted drugs. Since there is still a great deal that we must learn about cancer, it is critical that we continue to drive scientific discovery through innovative basic research.

Although cancer is being "unraveled" rapidly at the gene, protein, and even the "nano" levels by the largest group of basic cancer researchers who have ever investigated a specific disease, we have not concomitantly created the technology development resources and seamless system needed to capitalize on their discoveries. Ironically, our understanding of the causes of cancer and many other crippling and lethal human diseases has progressed so rapidly in the past few years that the Nation's biomedical research infrastructure is not organized to foster the development and integration of advanced technologies. Historically, the pathway between basic discovery and clinical application is often slow, tortuous, and expensive, with the cost of developing a new therapeutic drug projected to cost over $800 million and requiring up to 14 years. This is especially true for cancer, where clinical trials are complex and often long and markets for oncology products are generally small. Although we anticipate that the fruits of biomedical research eventually will enable the conquest of cancer, to realize the exponential progress against cancer that we believe possible will require adapting successful strategies from other fields that have faced a similar dilemma.

The history of the 20th century demonstrates that revolutionary advances in technology occur when resources are brought to bear at the interfaces between scientific disciplines. For example, fundamental discoveries in physics and chemistry provided the basis for the development of the early transistors and integrated circuits, but it took their convergence with engineering to create the semiconductor and microprocessor industries. These advances culminated in the computer revolution of the past 20 years and its virtually incalculable impact on the Nation's current and future prosperity.

The NCI believes that we are now at a similar inflection point in cancer and biomedical research, requiring a similar convergence of disciplines, organizations, and sectors, and the investment of resources to develop and deploy the advanced technologies needed to conquer cancer and many other diseases. The evidence for this inflection point in biomedical research is exemplified in an unimagined pace of change driven by the convergence of advanced technologies such as genomics, bioinformatics, chip technologies, proteomics, and nanotechnology with breakthroughs from basic research. For example, the cost of sequencing a gene has dropped from $150 in 1998 to less than $9 today, opening up the possibility of personal genome analysis. Capitalizing on this inflection point to produce exponential progress against cancer requires that we successfully integrate and leverage our now fragmented advanced technology development resources into a new seamless system that ensures the commercialization and delivery of targeted cancer diagnostics, therapies, and preventives to patients.

The NCI has already taken the first steps to achieve these paradigm-shifting goals through the launch of an unprecedented cancer bioinformatics platform, the Cancer Bioinformatics Grid (caBIG). The NCI will invest more than $25 million in the launch of this broad informatics "connectivity" platform in FY 2004, with additional investments of over $100 million in the next 4 years. We have also undertaken early efforts in areas such as proteomics and biomarkers, biosensors, and nanotechnology. The NCI has also invested in the development of

other common technology platforms that will be critical to the development of the NATIc concept, including a pilot program to establish standards for biorepositories, biomarker validation, and a re-engineered clinical trials system. However, unless we act to invest in a national network such as the NATIc, the effects of the NCI's strategic investments in these platform technologies will be limited.

Finally, it is logical to ask why the NCI cannot just shift its resources and focus to the creations of the NATIc. The fact is that with our current investments in cancer research, we are doing the right thing in Discovery of cancers' molecular mysteries and the Delivery of state-of-the-art interventions. What is now required is to complement and wed to this effort the Development of sophisticated technology tools that will exponentially accelerate the rate of progress. We must expand our efforts to include the development of a robust national capability to translate our basic scientific discoveries rapidly into innovative clinical applications. We can catalyze a "new era" in biomedical and cancer research, one in which the results of our past investments in basic and clinical research are optimally leveraged by an accelerated pace of advanced technology development to specifically detect, prevent, and treat cancer. The development of the NATIc is critical to achieving these goals and to the NCI's vision of eliminating suffering and death due to cancer in the next decade.

Chapter 2: The Future - Creating the NATIc

The NATIc Concept: The NCI believes that within a decade we can make certain cancer is no longer our greatest fear but is instead a manageable, non-lethal disease. To capitalize on heretofore unimagined advances in biomedical research opportunities and secure this future, the NCI proposes that we undertake the creation of the *National Advanced Technology Initiative for Cancer (NATIc).*

The NATIc will herald a new era in biomedical and cancer research that is fostered by technology. The NATIc will capitalize on the wide array of existing resources and capabilities nationwide for the development and commercialization of advanced technologies that are specifically designed or modified for application in biomedical research. Consisting of an unprecedented group of advanced technology "hubs" (clusters of organizations and institutions), the NATIc will be connected through common technology platforms such as bioinformatics, utilize advanced prototyping and other engineering capabilities, and work through advanced technology development teams. These interdisciplinary hubs will accelerate the application of current advanced technologies, integrate disparate technologies to create unique new platforms, and optimize the development and integration of new and emerging technologies.

The hubs may include academic medical and Cancer Centers, State and regional centers of innovation and biotechnology, national laboratories, and other qualifying entities. Each hub will qualify for funding on the basis of demonstrated excellence and capabilities in a specific area of advanced biomedical technology. The hubs will be virtually connected through a common bioinformatics platform, and all participating entities will be required to share all NATIc data, technology, and so on in real time with the entire network. The NATIc will provide direct access to unique, powerful platform technologies that no single center of excellence could afford, e.g., a national bioinformatics grid, and undertake the development of advanced technologies that cannot be achieved singly. The NATIc will solve "breakthrough" technology problems in areas ranging from the design and fabrication of new nanotechnology-based diagnostics, to integrated functional imaging of the effects of new classes of drugs on metastatic pathways in tumors, to the development of advanced structural biology to enable the design of targeted therapies for cancer and other diseases.

Role of the Cancer Centers: With significant technology development capabilities in areas ranging from advanced imaging to drug discovery to new diagnostics platforms, the NCI's Cancer Centers will be significant participants in the NATIc. Established after the signing of the National Cancer Act of 1971, the Cancer Centers are a unique national resource. There are currently 61 geographically disbursed NCI Cancer Centers. Institutions that have a Cancer Center represent more than 80 percent of all of the research supported through the NCI. To qualify as an NCI Cancer Center, these institutions must possess strengths in peer-reviewed basic and clinical research and, in most instances, deliver to the community state-of-the-art cancer care through clinical trials. The Cancer Centers are also central to the development, transfer, and commercialization of advanced technologies. In fact, targeted drugs such as Gleevec® (a molecularly targeted drug for chronic myelogenous leukemia) are often discovered and partially developed in the Cancer Centers before commercialization through entrepreneurial start-up companies or licensing to the private sector.

Leveraging Our National Investment in Biomedical Technologies: The NATIc will allow the NCI to leverage emerging State and regional investments in biomedical technology development for the express purpose of closing the discovery-to-development gap for cancer. The magnitude of these investments varies, but a few examples follow:

- Wisconsin is investing $317 million over 10 years in advanced biomedical technology development.
- Ohio is investing $250 million in biomedical research and technology development.
- Pennsylvania is investing $60 million annually in biomedical research and technology, has set up technology development "greenhouses," and has made a one-time investment to establish a venture capital fund to commercialize the State's advanced technologies.
- Michigan is investing $20 million per year for 20 years in its life sciences corridor.

Currently, 40 States are investing in biomedical innovation and biotechnology centers[1] and many are specifically supporting the translation and development of advanced technologies for cancer.

Many of these regional centers are funded through State appropriations and consist of a network of public and private partners working toward a goal of accelerating the movement of advanced technologies into new companies, which is directly tied to the growth of high-tech jobs on the local level. The NATIc will be well positioned to capitalize on these advanced technology capabilities as many of them "map" to regions/States that are directly aligned with the NCI's Cancer Centers and other qualified academic research institutions.

The NATIc hubs will have unprecedented opportunities to drive a wave of advanced technology development that will produce new start-up biotechnology companies and fuel a new regional and national biomedical technology-based economic development model. In several areas, the Cancer Centers (or other qualified academic research institutions) are already central to this rapidly developing network of State/regional biotechnology entrepreneurial and innovation initiatives. In the case of biotechnology, these State and regional clusters represent a geographic concentration of collaborating institutions and firms and their supplier network. These geographically dispersed biotechnology and innovation "clusters" represent an outstanding national resource base that will enrich the NATIc and accelerate its formation.

NATIc Hubs: The NATIc hubs will represent broad consortia with significant breadth and depth of technology development capabilities, while smaller nodes will focus on emerging technologies. Given their mandate, capabilities, and geographic distribution, it is expected that each consortium will include one or more of NCI's Cancer Centers (or other qualified academic research institutions). However, the integration and ongoing coordination of a NATIc advanced technology hub may be led by a range of qualifying entities including Cancer Centers, State/regional innovation or biotechnology clusters, and centers, academic medical centers, and foundations. Examples of the anticipated characteristics of these hubs include the following:

- Consortia with defined areas of designated technology innovations applicable to cancer and a track record in the identification, transfer, development, and commercialization of advanced technologies.
- An NCI Cancer Center (or other qualified academic research institutions) as the lead institution or as a member of the hub.
- Demonstrated advanced-technology workforce.
- Active participation by hub members in public-private partnerships.
- Membership of advanced technology centers such as the Department of Energy, National Aeronautics and Space Administration, or National Institute of Standards and Technology laboratories.

The NCI has identified a number of potential advanced technology focus areas for the hubs, including:

- **Bioinformatics and Advanced Computing.**
- **Advanced Imaging.**
- **Drug Discovery and High-Throughput Screening.**

[1]Laboratories of Innovation: State Bioscience Initiatives 2004, Battelle Technology Partnership Practice.

- **Proteomics, Biomarkers and Diagnostic Platforms.**
- **Computational and Systems Biology.**
- **Nanotechnology.**
- **High-Throughput Genomics Sequencing.**
- **Biopharmaceutical Development and Scale-Up.**
- **Biosensors and Model Systems Engineering.**
- **Bioengineering and Advanced Prototype Facilities.**

Examples of Potential Hubs: During the past year the NCI has initiated efforts to locate and "map" some of the major existing and emerging regional/State centers of biotechnology and innovation. In addition, the NCI brought a number of these regions together in January 2004 in a multi-sector meeting to discuss ways to close the discovery-to-technology development gap for cancer research. The meeting report "Leveraging Multi-Sector Technology Development Resources and Capabilities to Accelerate Progress Against Cancer," NIH Publication No. 04-5522 is available. The following represents a few examples of the developing "network of networks" which, along with NCI's Cancer Centers and other entities, can bring enormous technology development resources to bear in eliminating suffering and death due to cancer.

- ***Potential Hubs in Systems Biology and Biomarkers (Pacific Northwest Cluster).*** The Pacific Northwest region has more than 1,800 life scientists, robust investments in cancer technology development, and a number of successful biotechnology start-ups (e.g., Immunex, Rosetta, Zymogenetics, etc.). The Fred Hutchinson Cancer Research Center (FHCRC), University of Washington (UW), and the Institute for Systems Biology (ISB) conduct nationally recognized programs in cancer research, while information technology companies such as Microsoft and Intel provide unparalleled computational capabilities. The Department of Energy's Pacific Northwest National Laboratory (PNNL) is another key regional presence in advanced technology development. This cluster of institutions represents potential national hubs in key areas such as nanotechnology, biomarkers, proteomics and diagnostics, and bioinformatics.

  A key strategy for achieving NCI's 2015 goal is through earlier recognition of biomarkers of abnormal cells. A potential hub in biomarkers, proteomics, and diagnostics technologies is emerging from the combined capabilities/facilities of the FHCRC, PNNL, UW, and ISB along with several biotechnology companies. By developing and employing advanced mass spectrometry, immunology-based affinity systems, and advanced computing capabilities to detect abnormal proteins, this cluster promises to produce new technologies and companies to detect cancer at its earliest stages.

  This region is also emerging as a systems biology hub for assembling the vast knowledge about the molecular pathways of cancer. Experts in imaging, advanced technologies, nanobiology, microfluidics, and computational biology and clinical oncologists have assembled an advanced technology hub with demonstrated capability to achieve breakthroughs in cancer detection, drug discovery, and therapeutic monitoring, especially in the area of nanotechnology. The ability to measure and monitor thousands of events through nanosystems and imaging in cancer patients will be critical for the identification of targets needed to support the development of new cancer diagnostics, therapies, and preventives.

- ***Potential Drug Development and Clinical Trials Hub (Southeastern Pennsylvania Cluster).*** The Pennsylvania (including parts of New Jersey) cluster focuses on advancing drug discoveries from cancer research through commercialization. The region has a critical mass of regional Cancer Centers, pharmaceutical and biotechnology companies, medical colleges, medical research centers, and allied health programs. The major cancer research centers include Fox Chase Cancer Center, Thomas Jefferson University, Wistar Institute, and the University of Pennsylvania Cancer Center. Key private sector participants include Cephalon, DuPont Pharmaceuticals Company, Johnson & Johnson, Merck & Co., Sanofi-Synthelabo, Glaxo SmithKline, Aventis, AstraZeneca, Bristol-Myers Squibb, and Wyeth-Ayerst, Inc. A "greenhouse" project, supported through Pennsylvania tobacco settlement funds, fosters the development of early-stage biotechnology companies - a significant portion of which is cancer focused.

  This cluster is composed of four components: evidence-based medicine, patient support services, patient information systems, and regional contract research organizations—all connected through regional Cancer Centers. This model has the potential to accelerate the pace by which basic discoveries move into the clinic. Enabled by integrated information systems that range from basic discovery through clinical delivery, the cluster is supporting the emergence of a new trans-sector technology development and clinical trials pipeline. Biotechnology companies such as Cytogen, i-STAT, and the Liposome Company are developing advanced therapeutic approaches using imaging, biosensor, and targeted delivery approaches. Information technology solutions, from database mining to rapid online patient recruitment into clinical trials, are dramatically shortening timelines and reducing costs of clinical phase testing. This potential hub, known for its new funding models and commercialization strategies, promises to yield highly effective and efficient drug development and integrated clinical trials capabilities.

- ***A Potential Targeted Drug Discovery and Development Hub (San Francisco Bay Region Cluster).*** The San Francisco Bay region is the birthplace of biotechnology and home to Stanford University, University of California, San Francisco (UCSF), University of California, Berkeley, and Federal laboratories such as the Lawrence Berkeley National Laboratory (LBNL). The UCSF and LBNL united to create a regional Biotechnology Resource for Interdisciplinary Discovery and Genome Engineering (BRIDGE) that includes local biotechnology and pharmaceutical companies such as Cellomics and Affymetrix. The BRIDGE consortium has developed automated techniques to screen compounds for specific therapeutic responses. This potential hub has the capability to produce high-throughput, evidence-based, cellular "fingerprints" of drug candidates to accelerate cancer therapeutics discovery and development.

  Collaborators include investigators from Federal and State institutions, academia, and industry including expertise in cancer biology, physics, chemistry, engineering, computation, and biomedicine. The BRIDGE provides in-depth mechanistic information on drug candidates, develops diagnostic and predictive markers, and pursues novel therapeutic approaches. This approach to drug discovery and target validation will accelerate drug development by more precisely identifying patients who will respond, reducing clinical trial size and combining drugs that will produce synergistic effects. This potential hub also provides a wide array of advanced technologies, including nanofabrication.

- ***Potential Advanced Imaging and Nanotechnology Hubs (Ohio Cluster).*** With annual R&D investments of over $1 billion annually, Ohio represents a vast array of capabilities and expertise in advanced biomedical technologies. Major research and technology development centers include Case Western Reserve University, Ireland Cancer Center, University Hospitals, CASE Comprehensive Cancer Center, Cleveland Clinic Foundation, Ohio State University, and the University of Cincinnati. Advanced technology resources from its nonprofit and private sectors (e.g., Battelle Memorial Institute, Johnson & Johnson Corporation, and Procter & Gamble Pharmaceuticals) further support a long-standing culture of innovation.

The region could qualify for hubs in several areas, notably, advanced imaging and nanotechnology. This region also has significant strength in device development and advanced prototyping. Coordinated at the State government level through its Edison Centers, technology development programs to foster commercialization and entrepreneurship have created an environment that encourages and rewards innovation and technology development.

Convergence of the State's centers of excellence in electrical engineering and materials science offers the potential to rapidly accelerate the pace of technology development. Combining these engineering and physical science disciplines with expertise in chemical synthesis, photolithography, electrical engineering, and bioinformatics provides a strong focus for nanotechnology and diagnostic device development. Sophisticated capabilities in biosensors, nanocantilevers, nanowires, and nanoparticles offer the potential to contribute significantly in areas such as three-dimensional molecular imaging, protein identification, and multicomponent and targeted delivery of molecules.

The Coordinating Hub: The NCI-Frederick as the DHHS' only Federally Funded Research and Development Center (FFRDC) is well suited to serve as the coordinating hub for the NATIc through its contracting mechanisms, integrated distribution networks for data, animal models, specimens and reagents, and platform technology capabilities. NCI-Frederick was established in 1972 as a FFRDC and operates as a GOCO (government owned/ contractor operated) installation. Frederick's classification as an FFRDC also affords the NCI a range of unique procurement and response capabilities to support the NATIc Strategic Technology Development Program.

The decision to provide certain core resources to all of the hubs will be based on the costs of reproducing certain unique resources across the network. Some resources, such as certain biologics, unique biospecimens, and/or prototyping and engineering capabilities, may be most cost-effectively and efficiently provided centrally. Special services such as pharmaceutical scale-up can also be made available through the coordinating hub. The programs at NCI-Frederick represent a unique national resource that can serve as an important facilitative bridge to develop the NATIc and hasten the translation of findings from basic research into clinical application.

NATIc Operations Plan

Chapter 3: NATIc Operations Plan

Overview of the NATIc Network: As planned, the NATIc will consist of up to 10 State/regional technology hubs. On the basis of the NCI's preliminary assessment of possible State/regional hubs, the average number of entities per hub will be approximately five. Therefore the program has the power to eventually link, coordinate, and synergize over 50 entities or facilities around the Nation. To qualify for funding, a hub must clearly demonstrate excellence in a specific area of advanced technology development as assessed by rigorous peer review. The hubs will be awarded competitively with funds flowing directly to all members of the winning consortia. For budget purposes, it is assumed that each participating entity would be funded for up to 5 years, depending on the achievement of specific milestones. The NATIc will also fund a limited number of free-standing emerging technology nodes in selected organizations to ensure the entry of new technologies into the hubs. There are funding mechanisms and program strategies that the NCI has over 30 years' experience in creating and managing.

Each of the hubs will consolidate a critical mass of specialized resources and capabilities to create an unparalleled capability in a specific technology development area. The integrated network will represent a new national advanced technology development enterprise. The hubs will qualify in specific areas of advanced technology development. Examples of anticipated technology focus areas for hubs include:

- **Bioinformatics and Advanced Computing.**
- **Advanced Imaging.**
- **Drug Discovery and High-Throughput Screening.**
- **Proteomics, Biomarkers and Diagnostic Platforms.**
- **Computational and Systems Biology.**
- **Nanotechnology.**
- **High-Throughput Genomics Sequencing.**
- **Biopharmaceutical Development and Scale-Up.**
- **Biosensors and Model Systems Engineering.**
- **Bioengineering and Advanced Prototype Facilities.**

Current advances in information technologies (and bioinformatics) will allow the NATIc to operate as an integrated, coordinated technology development and deployment center for the Nation. To optimize NATIc management, each of the individual hubs and nodes will interface directly with all of the others in real time by participation in an information technology grid (caBIG) established by NCI. All of the participating hubs and nodes will be directly linked to the NATIc's coordinating center, which will be located at the NCI's FFRDC in Frederick, Maryland.

Management and Governance: The NATIc will operate as an integrated distributed nationwide network of technology "hubs" and "nodes" with a central coordinating unit. The hubs will comprise consortia of cancer and academic centers, State/regional technology innovation centers, and private companies and, in selected cases, national laboratories.

The overall management of the NATIc's virtually connected and integrated network will occur at three levels:

- *NATIc Intra-hub Management and Coordination Group.* A successful hub will be required to present an intra-hub coordination and management plan and organization that will oversee the functions of the hub. Each of the advanced technology hubs will designate a lead organization for the purposes of competing to be selected to become part of the NATIc network. Since the hubs will propose to lead a specific area of advanced technology development (in the areas previously defined), each consortium must present a

plan for its coordination and management. This plan must detail the administrative structure and function and show how the participating entities will integrate their respective capabilities into a functioning whole. In addition, they must also present a construct for interacting with the other hubs, the Senior Technical Council, and the Coordinating Center. Formal interfaces with the NCI's NATIc Program Management Group will be pre-defined. All hubs will be evaluated on the basis of achieving milestones in their specific technology focus area.

- *NCI's Program Management Group.* The NCI's NATIc program managers will work with individual hubs to set up all aspects of the program, establish milestones in collaboration with the hubs and the Senior Technical Council, and monitor investments versus achievement of milestones. They will also lead site visits and receive technology platforms, prototypes, and other deliverables. The productivity of all hubs and network operations will be reviewed, and a report presented annually.

- *Senior Technical Council.* This body will oversee the governance of the NATIc. It will include NCI's leadership, Program Managers, and representatives from all of the hubs comprising the network. The scope of the functions of this group will include participation in priority-setting for the hubs and the identification of mission-critical technology needs. The Senior Technical Council may also advise on milestone achievement for hubs and cross-hub technology development teams.

The NATIc Culture: The NATIc will be a magnet for innovative scientists, clinicians, and engineers from the government and academic and private sectors who enjoy working in multidisciplinary teams and developing and using state-of-the-art enabling technologies. The purpose of the NATIc's governance and management is to connect leading scientists from core biological research areas with investigators from chemistry, physics, engineering, mathematics, and information technology to solve problems that represent key barriers to progress against cancer. These interdisciplinary teams will have unique access to the expertise and capabilities resident in the overall network, including clinical resources within the hubs. Investigators in all the hubs will have the capability of moving their concepts through the development phase to proof of concept and, potentially, prototyping.

Many of these scientists and engineers may not currently work in cancer research, so each hub will be challenged to attract new institutions and talent. The environment of the NATIc will provide unprecedented opportunities for cross-disciplinary interaction and information exchange. Problem-oriented "tiger teams" will be a common approach to achieving breakthroughs that will lead to revolutionary new diagnostic, therapeutic, and preventive interventions for cancer.

Role of the NCI Coordinating Center: The NATIc Coordinating Center will be located at the National Cancer Institute-Frederick (NCI-Frederick), a Federally Funded Research and Development Center (FFRDC) that currently coordinates a range of technology and research resources across the cancer research enterprise.

The NATIc Coordinating Center will promote common standards and provide core resources to the member hubs and nodes and to the community at large. Strategically, the NCI-Frederick is well suited to achieving these goals through its contracting mechanisms, integrated distribution networks for data, animal models, specimens, and reagents, and platform technology capabilities. The NCI-Frederick Coordinating Center represents a unique national resource that can serve as an important facilitative bridge to support all of the hubs in the NATIc network (**Figure 3-1**).

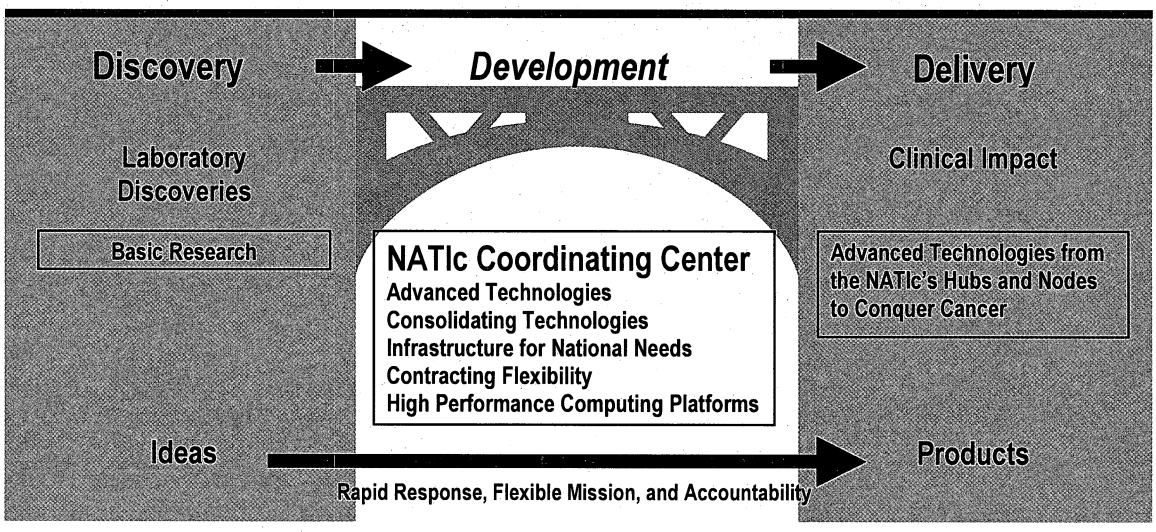


Figure 3-1. NCI-Frederick Coordinating Center

The NCI-Frederick Coordinating Center will serve two major roles that provide unique value to the national network. It will provide contracting authorities to support the Strategic Technology Development Program and access to unique core resources. Resource availability for all NATIc members will be determined on the basis of costs. For example, the centralized availability of certain biologics, unique biospecimens, and/or prototyping and engineering capabilities to all hubs represents resources that may be most cost-effectively and efficiently provided through the Coordinating Center. The availability of certified good manufacturing practices (cGMP) and engineering/prototyping facilities within the Coordinating Center (and selected NATIc hubs) will allow investigators to scale up drugs and biologics, create working models of potential new diagnostics, and evaluate new diagnostic and therapeutic agents in clinical trials. In addition, NCI could provide access to integrated activities with other Federal agencies, e.g., FDA.

The Strategic Technology Development Program: In addition to their specific areas of technology development responsibilities, the hubs and nodes will compete to lead selected advanced technology programs to address specific problems in cancer therapy, diagnosis, and prevention. For the Strategic Technology Development contract portion of the program, NATIc teams would bid to develop a specific technology platform, with planning or developmental funding allocated initially to more than one team. Each of the teams will be evaluated on the basis of meeting the milestones defined for the program. Ultimately, one or more teams will be selected on the basis of their original plan and success in satisfactorily achieving their milestones for more substantial funding to complete the development of the advanced technology platform specified by the contract. Funding would be discontinued for certain projects if milestones were not achieved. These entities would be free to bid on the development of additional technology platform as they determine appropriate.

The Strategic Technology Development Program would focus on the identification of the advanced technology platforms needed to accelerate progress in critical areas of the diagnosis, treatment, and prevention of cancer. The specific definition of these technology requirements would be determined by the governance and management of the NATIc through a process that would seek significant input from across the entire biomedical research enterprise. The following represents some examples of potential focus areas for this competitive funding mechanism:

- Nanotechnology platforms to detect early cancer, deliver targeted therapies, or monitor responses.
- Advanced drug-screening platform that integrates robotics-supported chemistry, nanotechnology, informatics, and high-throughput assays.
- Molecularly targeted therapies.
- National "smartcard" supported clinical trials resource.

Intellectual Property Management: The advanced biomedical technologies that will derive from the NATIc unquestionably hold the promise to significantly impact cancer and accelerate the realization of a personalized medicine-based 21st century health care system. In achieving these goals, the NATIc will generate significant opportunities to develop and commercialize bioscience inventions through licensing, partnerships, and new start-up companies. These activities also hold real promise for enhanced economic development in the States and regions in which the advanced technology hubs reside. However, to achieve these technical and economic goals will require a well-thought-out strategic plan for managing the intellectual property of the NATIc.

Because many of the technology projects conducted through the NATIc will involve multiple advanced components (probes, chips, arrays, genes and proteins, small molecules, etc.), strategies that streamline collaborations among participating entities and enable rapid technology handoffs will be crucial. One of the current encumbrances to current technology development is exclusive licensing of technologies that individually have no commercial value. The NCI will implement non-exclusive and cross-licensing strategies to ensure pre-competitive (public domain) intellectual property through its policies, contracts, and other agreements. These strategies will maximize the availability of pre-competitive technologies while ensuring the ability of the NATIc to create integrated technology platforms. The hubs will benefit significantly from the commercialization of these broad platforms and will also be free to establish new intellectual property for commercialization.

Several types of collaborative research relationships and partnership with other government agencies, academia, and private sector organizations will be required for the NATIc to reach its full potential as a national resource for the development of biomedical technologies. Many of these relationships can be formed through existing mechanisms and legislative authorities. However, new legislation and/or practices and procedures may be required to permit all envisioned relationships. NCI will work with the Office of Technology Transfer at the NCI and the NIH to review and strengthen these policies. The goal is to fully maintain the core principles of the Bayh-Dole Act, while facilitating the interchange of basic advanced technology components among participating entities within the hubs and throughout the network.

Intellectual Planning and Oversight. In planning for the intellectual property management for the NATIc, NCI met with national experts in biotechnology development, licensing and technology transfer, commercialization strategies, and entrepreneurship programs. Experts from the Association of University Technology Managers (AUTM), the Wisconsin Alumni Research Foundation (WARF), Massachusetts Biotechnology Council, New Economic Strategies, Burrill & Co., the Ewing Marion Kauffman Foundation, and national academic leaders in health economics and technology development have provided input into the NCI's initial intellectual property strategic planning for the NATIc. The goal of this plan is to ensure maximum public benefits while also maximizing opportunities to establish partnerships for commercialization. In addition, these experts are advising the NCI on those technology transfer and licensing best practices that will become the foundation for a NATIc training program.

Prior to establishing the NATIc hubs, the NCI will formally constitute an advisory board of experts in technology management, commercialization, legal, and venture funding issues. This body would make recommendations on the NATIc's intellectual property and commercialization principles and strategies and subsequently serve in a review and advisory role. This board will also be charged to make recommendations on needs for changes in existing policies and regulations. A central database for facilitating technology transfer and exchange of materials among all entities in the hubs will be provided through caBIG.

Key NATIc Intellectual Property Management Principles and Mechanisms. The NCI has extensive experience with technology development programs that maximize the availability of pre-competitive data and knowledge while protecting the ability of domain experts to create robust patents. It is anticipated that several of these strategies will be effective in managing the array of intellectual challenges presented by the NATIc as follows:

- Determination of Exceptional Circumstances (DEC) and Deviated Federal Acquisitions Regulations (FAR) Clauses Authorities. On a limited basis, NIH has the authority to restrict or limit the right to title for new inventions to ensure that critical inventions that will benefit the overall research enterprise are placed in the public domain. Currently, NIH uses these authorities narrowly, but it is anticipated that a DEC will be developed for selected intellectual property that derives from the NATIc hubs and nodes, especially in the area of assembly of components to produce an integrated advanced technology device or drug.
- Non-exclusive cross-licensing agreements across the NATIc.
- NATIc Transfer Agreement (NTA) for the exchange of research materials.
- Licensing Agreements to meet the goals of the NATIc.

Summary: The NATIc will capitalize on our prior investments in biomedical research; capture advanced technologies from the NCI's Cancer Centers and other academic institutions; leverage State and regional investments and strengths in innovation, technology development, and entrepreneurship; and increase the engagement of venture capital and the private sector in commercializing the products needed to detect, prevent, and treat cancer. Management planning for the NATIc seeks to optimize and integrate these capabilities and harness the expertise of every hub for the express purpose of accelerating the development and deployment of advanced cancer technologies. Directed advanced technology development programs will leverage the unique resources of the NATIc to solve "breakthrough" problems in areas ranging from design and fabrication of new nanotechnology-based diagnostics, to integrated functional imaging of new drugs in patients, to design of targeted therapies for cancer. Success in all the NATIc's programs will be measured on the basis of achieving key milestones.

Funding Sources and
Budget Plan for the NATIc

Chapter 4: Funding Sources and Budget Plan for the NATIc

It is proposed that the NATIc be launched in FY 2006 using an innovative combination of funds that will be outlayed to the more than 50 entities that comprise its hubs and nodes. **Figure 4-1** illustrates the overall organization of the NATIc in terms of sources of funds, NCI program development and management, and the disbursement of resources to the 10 advanced technology hubs and a selected number of specialized technology nodes. The figure also illustrates the dynamic nature of the NATIc, which will operate as a virtual, interactive, collaborative network where ideas, information, and technologies will flow throughout the overall system in real time.

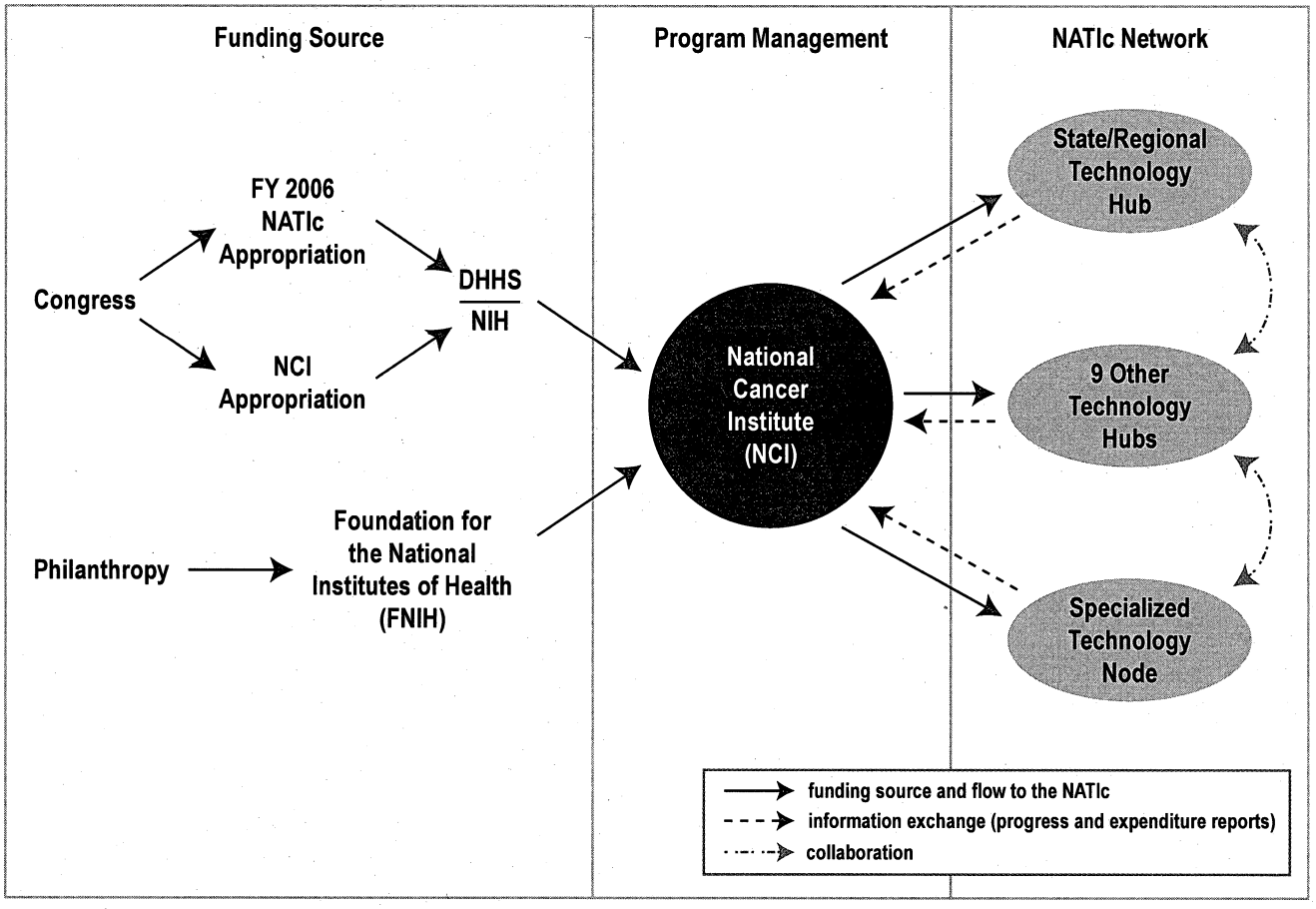


Figure 4-1. NATIc Organization and Funding Streams

Sources of Funds: As shown in **Figure 4-2**, a combination of Federal Government and private and institutional philanthropy will constitute the funding sources for the NATIc. Overall, 60 percent of the resources will be available via an annual Appropriation of $300 million per year in FY 2006 through FY 2010.

The NCI will also redeploy $0.1 billion each year for 5 years to support the NATIc from the Federal annual Appropriation already provided to the NCI. The NCI will continue to support the NATIc at a level not to exceed $0.1 billion per year at the point that the final NATIc Appropriation expires.

In addition, $0.5 billion will be raised in philanthropic funds to support the NATIc through the Foundation for the National Institutes of Health, Inc. (FNIH). Established by Congress as the National Foundation for Biomedical

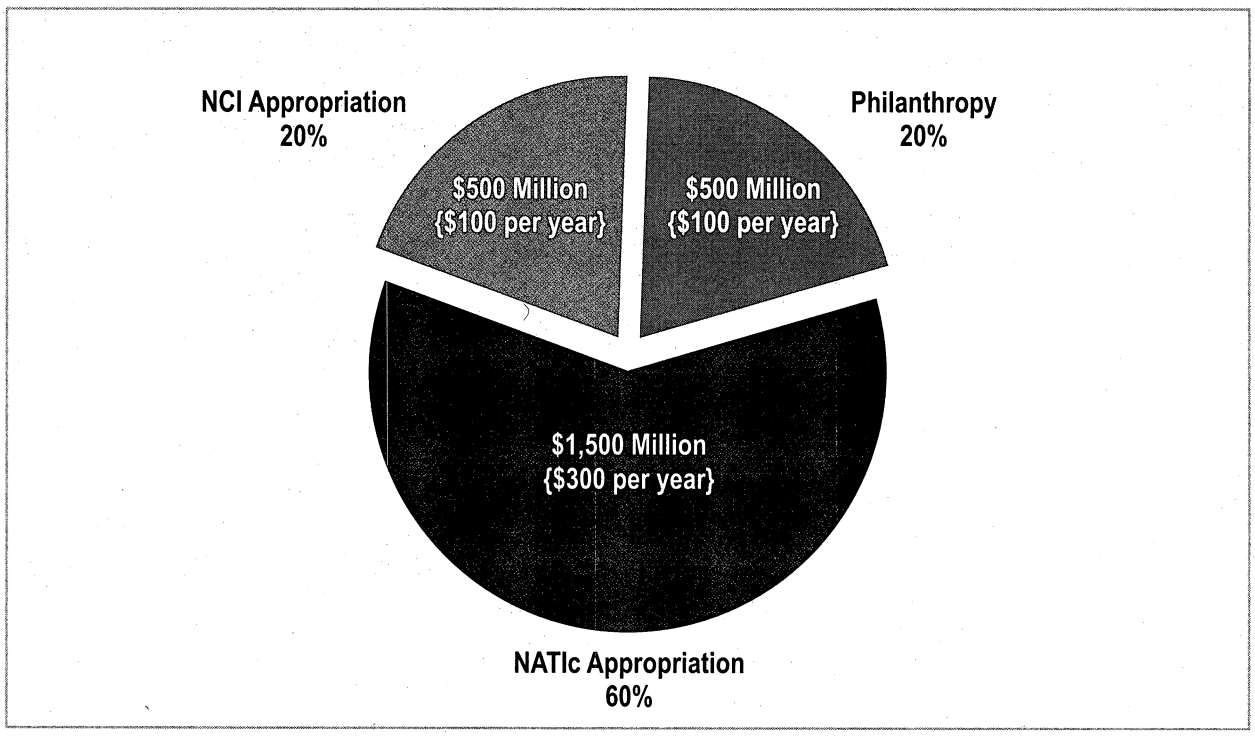


Figure 4-2. Funding Sources FY 2006 - FY 2010 for the National Advanced Technology Initiative for Cancer

Research, the Foundation was incorporated in 1996 as a 501(c)3 nonprofit organization. It has an independent board of directors of eminent scientists and representatives of industry and philanthropy. The FNIH will conduct a campaign feasibility study prior to beginning fund-raising and present a report to the board of directors. This phase allows FNIH to develop and refine strategies for engaging private sector entities to partner with the public sector to support the NATIc. The vision and scope of the project is shared with selected interviewees to assess interest and followed by direct interviews. Through this approach, FNIH and NCI will work together to develop an effective funding partnership to support the core mission of the NATIc.

NCI Program Development and Management: As shown in **Figure 4-1**, all funds for the NATIc will flow through the programmatic elements of the NCI. **Table 4-1** summarizes the array of NCI program activities that will be required, including the establishment and funding of the advanced technology hubs and the Strategic Technology Development Program that will be performed through the efforts of these consortia. Hubs will be monitored for meeting milestones in their specific areas of technology focus (e.g., advanced imaging, nanotechnology, drug discovery, etc.) and in their completion of specific contract and grant tasks designed to create specific technologies and prototypes. As the Coordinating Hub, the NCI's Federally Funded Research and Development Center (FFRDC) at Frederick, Maryland, will provide a range of services and technical resources to support the NATIc network. The FFRDC will also provide access to expanded contracting authorities that will be selectively employed to ensure that the work of the NATIc can proceed efficiently and on schedule.

Table 4-1. Description of NCI Program Activities
• Issue Request for Applications and Proposals. • Receive Applications and Proposals From Organized Technology Hubs/Nodes. • Conduct Special Peer Review of Applications and Proposals. • Prioritize Applications and Proposals and Make Funding Decisions. • Establish Fiscal Accounts for Hubs/Nodes. • Award Grant/Contracts for Strategic Technology Development Program. • Monitor Programmatic Performance Through Achievements of Milestones. • Monitor Business Management Performance. • Utilize Federally Funded Research and Development Center as Coordinating Hub. • Utilize Federally Funded Research and Development Center Authorities.

The relative distribution by percentage of NATIc funds into the major functions that will constitute the working virtual network and the NCI management components is shown in **Figure 4-3**. The major organizational unit of the NATIc will be the State/regional technology hubs. Each hub will represent a consortium of four to six organizations and institutions. As shown, 94 percent of the funding for the NATIc will ultimately be obligated and distributed to the extramural community. Through these advanced technology hubs, and the specific projects that they undertake through the Strategic Technology Development Program, the NATIc will develop and disseminate the 21st century medicines and devices needed to eliminate the suffering and death due to cancer in the next decade. The NATIc will fund approximately 10 State/regional technology hubs.

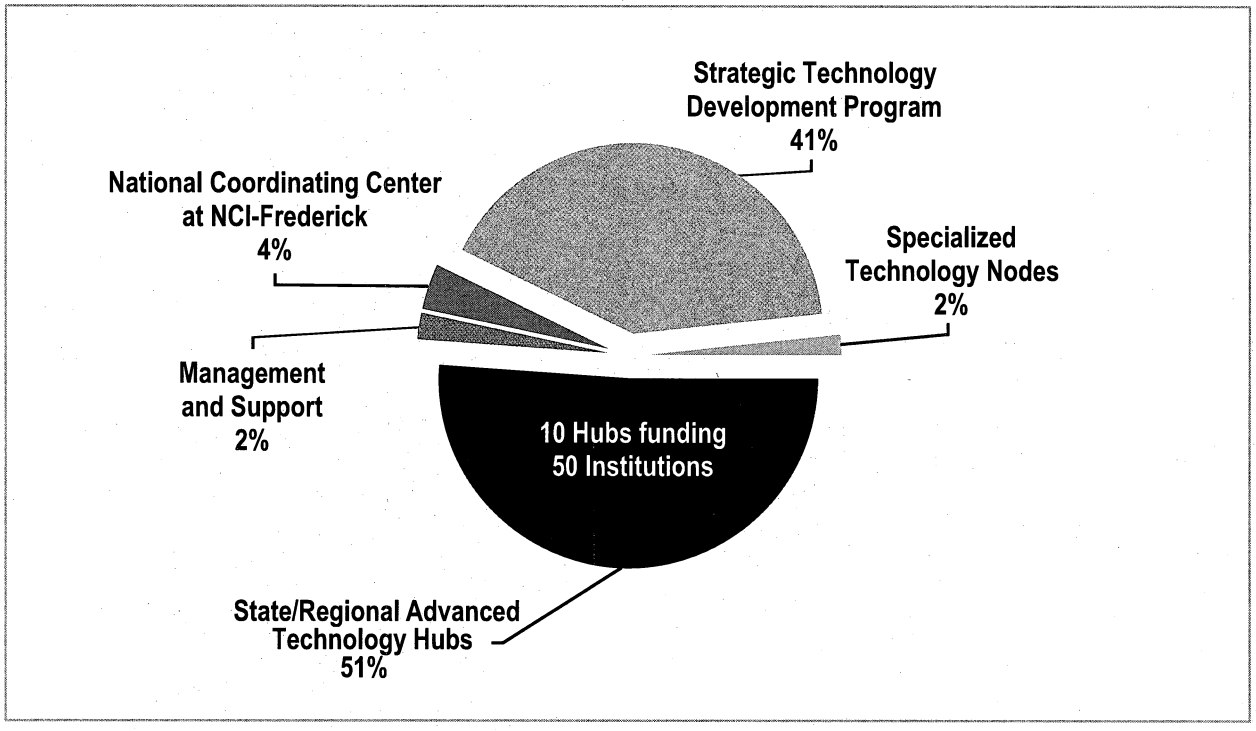


Figure 4-3. Distribution of Funding by Function for the National Advanced Technology Initiative for Cancer

These 10 hubs will include up to 50 participating entities from States and regions across the United States. As outlined in Chapter 2, these advanced technology hubs may be led by NCI's Cancer Centers, academic medical centers, engineering schools, State and regional centers of biotechnology and innovation, or other qualifying nonprofit organizations. Each consortium (hub) will designate a technical coordinator that will serve as the focus for technical planning and reporting. Each hub will have a technical planning committee to coordinate the function and output of the hub and interface its activities with those of the NCI's NATIc Senior Technical Council that will prioritize technology program needs and provide input on progress. Each hub will be overseen and milestones evaluated by an NCI program manager in coordination with the Senior Technical Council. Funding for the hubs will represent 51 percent of the total funding, with specialized technology nodes anticipated to be few in number, requiring 2 percent of the budget. The Strategic Technology Development Program will constitute 41 percent of the funds, and the costs of the coordinating hub and management represent the 6 percent remainder of the budget.

Chapter 5: Overall Budget, Obligations, and Outlays

The obligation and outlay of funds for the NATIc will begin in FY 2006. A summary of the recommended availability of funds, obligations for specific aspects of the NATIc, and the outlays to achieve the goals of the NATIc are shown in **Table 5-1**.

Table 5-1. Summary of Funding Sources, Obligations, and Outlays for the National Advanced Technology Initiative for Cancer (dollars in millions)

FUNDING SOURCES	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
NATIc Appropriation	$300	$300	$300	$300	$300	$1,500
NCI Appropriation	100	100	100	100	100	500
Philanthropy	100	100	100	100	100	500
Total Funds	**500**	**500**	**500**	**500**	**500**	**2,500**

OBLIGATIONS	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
State/Regional Advanced Technology Hubs 1/	$205	$268	$269	$269	$269	$1,280
Specialized Technology Nodes 2/		10	10	10	10	40
Strategic Technology Development Program 3/	266	191	190	191	191	1,029
National Coordinating Center at NCI-Frederick	20	20	20	20	20	100
Management and Support 4/	9	11	11	10	10	51
Total Obligations	**500**	**500**	**500**	**500**	**500**	**2,500**

OUTLAYS	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011-FY 2014	Total
State/Regional Advanced Technology Hubs	$83	$159	$215	$251	$266	$306	$1,280
Specialized Technology Nodes		4	7	9	10	10	40
Strategic Technology Development Program	106	144	177	192	196	214	1,029
National Coordinating Center at NCI-Frederick	9	14	17	19	20	21	100
Management and Support	8	11	11	10	10	1	51
Total Outlays	**206**	**332**	**427**	**481**	**502**	**552**	**2,500**
Portion from Federal Funds	**{166}**	**{267}**	**{342}**	**{385}**	**{402}**	**{438}**	**{2000}**

1/ Total number of entities funded: 50 within 10 State/regional advanced technology hubs.

2/ Total number of entities funded: 10 within 5 specialized technology nodes.

3/ The authority to make awards utilizing the "Other Transaction" authority should be included within the NATIc Appropriation.

4/ An increase of 30 FTEs to the current FTE ceiling would be required to perform inherently governmental functions.

Obligations of funds will be directed through four distinct categories of awards **(Table 5-2)** that represent the functions of the NATIc. The advanced technology hubs (State/regional technology hubs), specialized technology nodes, and the National NATIc Coordinating Center, located at the DHHS FFRDC at Frederick, Maryland, will make up the basic distributed network that will comprise the foundation infrastructure of this initiative.

Once qualified and funded, the hubs will be eligible to bid on specific Strategic Technology Development Programs. This program will be coordinated and managed through the NCI's program management structure for the NATIc and take advantage of the expanded authorities provided through the Coordinating Hub at the FFRDC. Each of the projects funded through the Strategic Technology Development Program will be defined in terms of the advanced technology deliverable required, and each successful bidder will be required to meet milestones and deliver a product or prototype technology at the conclusion of a specific program. Design and management of the advanced technology hubs and specialized technology nodes, monitoring of milestones, and priority setting will occur through a combination of NCI program staff and the Senior Technical Council, which will include representatives of all of the hubs comprising the network.

Table 5-2. Summary of Obligations by Function for the National Advanced Technology Initiative for Cancer (dollars in millions)

	Total for Program FY 2006-2010			
Advanced Technology Hubs and Nodes:	NATIc Appropriation	Philanthropy	NCI Appropriation	Total
State/Regional Advanced Technology Hubs	$1,280			**$1,280**
Specialized Technology Nodes		$10	$30	**40**
National Coordinating Center at NCI-Frederick			100	**100**
Subtotal Hubs and Nodes	**1,280**	**10**	**130**	**1,420**
Strategic Technology Development Program	220	490	319	**1,029**
Management and Support			51	**51**
Total Obligations	**1,500**	**500**	**500**	**2,500**
Obligations per year	***$300***	***$100***	***$100***	***$500***

Distribution of Funds by Mechanism: Illustrated in **Figure 5-1** is the distribution of funds by percentage and specific dollar amounts to be funded through the four mechanisms anticipated for the NATIc. Funding the consortia of institutions that will comprise the hubs will require other transactions authority (38 percent), as will certain of the Strategic Technology Development Program. Funds for this program will flow through both NCI's normal contract mechanisms and also the FFRDC mechanism to provide the flexibility needed to implement the Strategic Technology Development Program. Technology research grants (9 percent) will be managed through normal NCI processes.

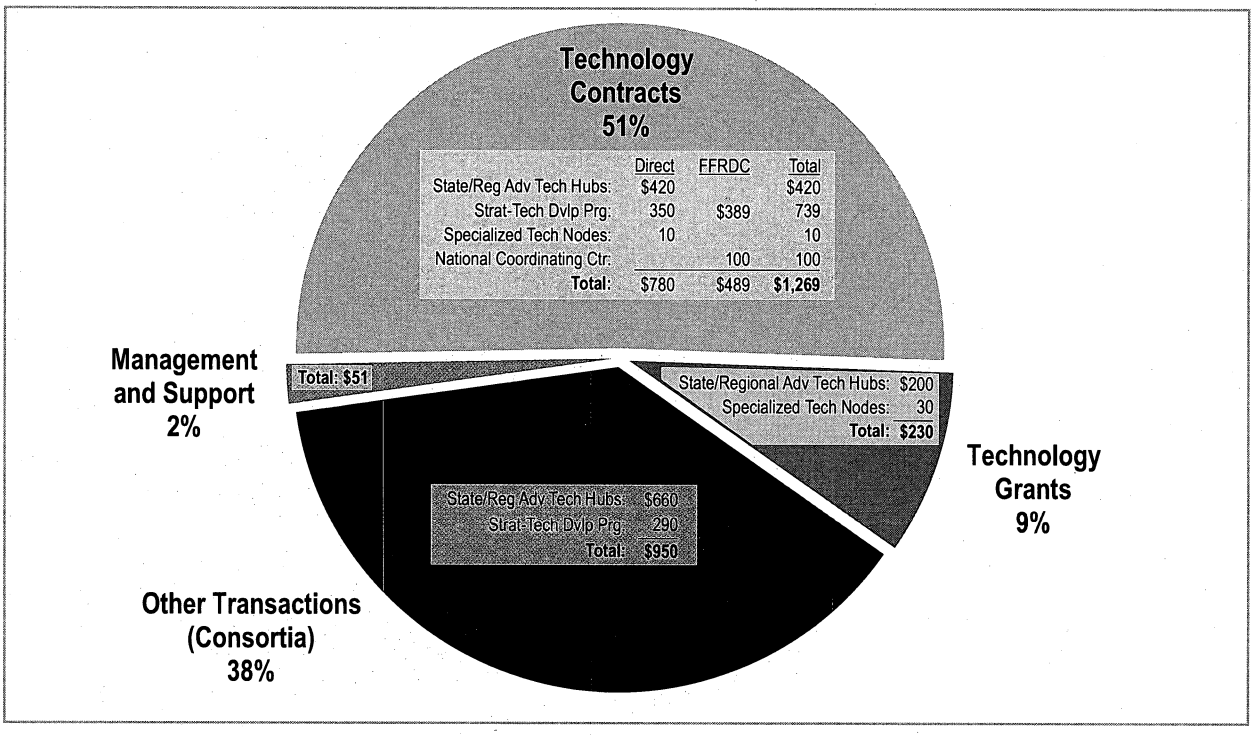


Figure 5-1. Funding by Mechanism for the National Advanced Technology Initiative for Cancer (dollars in millions)

The mechanisms proposed to establish and implement the hubs and Strategic Technology Development Program are a new model specifically designed to optimize the creation of innovative, targeted cancer therapeutics, diagnostics, and preventive agents. Meeting the goals of NATIc will require significant flexibility in terms of a milestone-driven evaluation approach for both the hubs and the Strategic Technology Development Program. For example, all of the teams chosen from those that successfully bid to develop specific technology platforms will perform for a period of time sufficient to evaluate their probability of success. From the teams that begin, one or two will be chosen to continue to develop a tangible prototype. This means that selected teams will be terminated and can bid on additional tasks emanating from the Strategic Technology Development Program. Funding would also be reduced or terminated to any hub that does not meet mission-critical milestones for its specific technology focus area.

All programs, including qualification and approval of the hubs, will be subjected to a peer review process and awarded on merit. Hubs will be evaluated on the basis of meeting milestones within the context of the advanced technology focus of a specific consortium, and contract performance on the Strategic Technology Development Program will be measured through both the achievement of technical milestones and the delivery of a final advanced technology and/or product.

The total funding for each of the major functions of the NATIc and the major mechanisms that will be employed to achieve the goals of each one is further demonstrated in **Table 5-3**. As described in **Figure 5-1**, **Table 5-3**, and Appendix B, Other Transactions Authorities will be used for the State/regional technology hubs and the Strategic Technology Development Program. The overall requirement for Other Transactions represents approximately 38 percent of the total required for the program. To further demonstrate the relationships between obligations of funds by activity to funding sources and mechanisms, a **detailed crosswalk of obligations by function to funding sources for FY 2006-2010 is shown in Appendix A**.

Outlay Rates for Distribution of NATIc Funds: The nature of advanced technology development and the critical need for rapid progress requires that the NCI employ outlay rates during the launch and implementation of the NATIc that will quickly create an unprecedented network of advanced technology hubs and provide novel mechanisms for programmatic support. The outlay rates proposed to achieve these goals are shown in **Table 5-4**.

Table 5-3. Crosswalk of Function, Source of Funds, and Mechanism (dollars in millions)

Summary - Obligations

Mechanism	Funding Source: NATIc Appropriation	Philanthropy	NCI Appropriation	Total	Percent Share
Technology Grants	$200		$30	$230	9%
Other Transactions (Consortia)	680	$140	130	950	38%
Technology Contracts	620	360	289	1,269	51%
Management and Support			51	51	2%
Total Obligations	1,500	500	500	2,500	100%
Obligations per Year	*$300*	*$100*	*$100*	*$500*	

Detail by Function - Obligations

Function/Mechanism	Funding Source: NATIc Appropriation	Philanthropy	NCI Appropriation	Total
Advanced Technology Hubs and Specialized Technology Nodes:				
State/Regional Advanced Technology Hubs	$1,280			$1,280
Other Transactions (Consortia)	{660}			{660}
Technology Contracts Direct	{420}			{420}
Technology Grants	{200}			{200}
Specialized Technology Nodes		$10	$30	40
Technology Grants			{30}	{30}
Technology Contracts Direct		{10}		{10}
National Coordinating Center at NCI-Frederick			100	100
Technology Contracts via FFRDC			{100}	{100}
Subtotal Hubs and Nodes	1,280	10	130	1,420
Strategic Technology Development Program	220	490	319	1,029
Other Transactions (Consortia)	{20}	{140}	{130}	{290}
Technology Contracts Direct		{350}		{350}
Technology Contracts via FFRDC	{200}		{189}	{389}
Management and Support			51	51
Management and Support			{51}	{51}
Total Obligations	1,500	500	500	2,500
Obligations per Year	*$300*	*$100*	*$100*	*$500*

Table 5-4. Summary of Outlay Rates Used for Analysis for the National Advanced Technology Initiative for Cancer

	1st Year	2nd Year	3rd Year	4th Year	5th Year
State/Regional Advanced Technology Hubs	40%	65%	85%	96%	100%
Specialized Technology Nodes	40%	65%	85%	96%	100%
National Coordinating Center at NCI-Frederick	45%	70%	85%	96%	100%
Strategic Technology Development Program	40%	65%	85%	96%	100%
Management and Support	89%	100%	100%	100%	100%

It should be noted that these rates allow for early identification of the advanced technology hubs and facilitate establishment of the management structure. The goal is to outlay most of the funds during the first 5 years of the program to accelerate development of the needed technologies and capitalize on discoveries.

The $2.5 billion of Federal and philanthropic funds will be outlayed or disbursed following all Federal requirements and in accordance with the standard Federal outlay payment system. The rate of outlays in a given year, compared with the obligations, will vary depending on the timing and nature of the award. The outlay or cash payback to the institutions compared with the obligations in the first year of an award would approximate 40-45 percent of the obligations. The remaining 60 percent will be outlayed from the Federal Treasury over the following 4 years until the full legal obligation is met.

Outlay Analysis: As shown in **Table 5-5**, the NCI will strategically fund the hubs during the first years of the program so that the rate of progress needed both to create technologies in their area of focus and to respond to technology development opportunities is maximized. The NATIc will provide an unprecedented source of advanced technologies that will fuel intellectual property creation, licensing, and new partnerships between participating institutions and the private and philanthropic sectors. It is anticipated that the NATIc will encourage the region/State centers of innovation and biotechnology to increase their investment in these critical areas to maximize high-technology job creation and economic development. The State and regional bioeconomic models that will be fueled by the NATIc promise to provide an opportunity for the NCI to "sunset" its ongoing funding after FY 2014. However, if needed, the NCI would continue to invest at a level of $100 million per year to ensure stability beyond this point.

Table 5-5. Summary of Outlay Analysis for Obligations - FY 2006 - FY 2014 (dollars in millions)

Outlays by Funding Source	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011-FY 2014	Total
NATIc Appropriation	$121	$196	$255	$288	$301	$339	$1,500
Philanthropy	40	65	85	96	100	114	500
NCI Appropriation	45	71	87	97	101	99	500
Total	**206**	**332**	**427**	**481**	**502**	**552**	**2,500**

Outlays by Function (includes all funding sources)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011-FY 2014	Total	Percentage of Total
State/Regional Advanced Technology Hubs	$83	$159	$215	$251	$266	$306	$1,280	51%
Specialized Technology Nodes		4	7	9	10	10	40	2%
National Coordinating Center at NCI-Frederick	9	14	17	19	20	21	100	4%
Strategic Technology Development Program	106	144	177	192	196	214	1,029	41%
Management and Support	8	11	11	10	10	1	51	2%
Total	**206**	**332**	**427**	**481**	**502**	**552**	**2,500**	100%

Figure 5-2 shows the annual obligations and planned outlay rates for NATIc. The peak outlay rate will be approximately $500 million per year in years 4 and 5 of this initiative. The outstanding balance of outlays from obligations made in prior years will be made in FY 2011 through FY 2014.

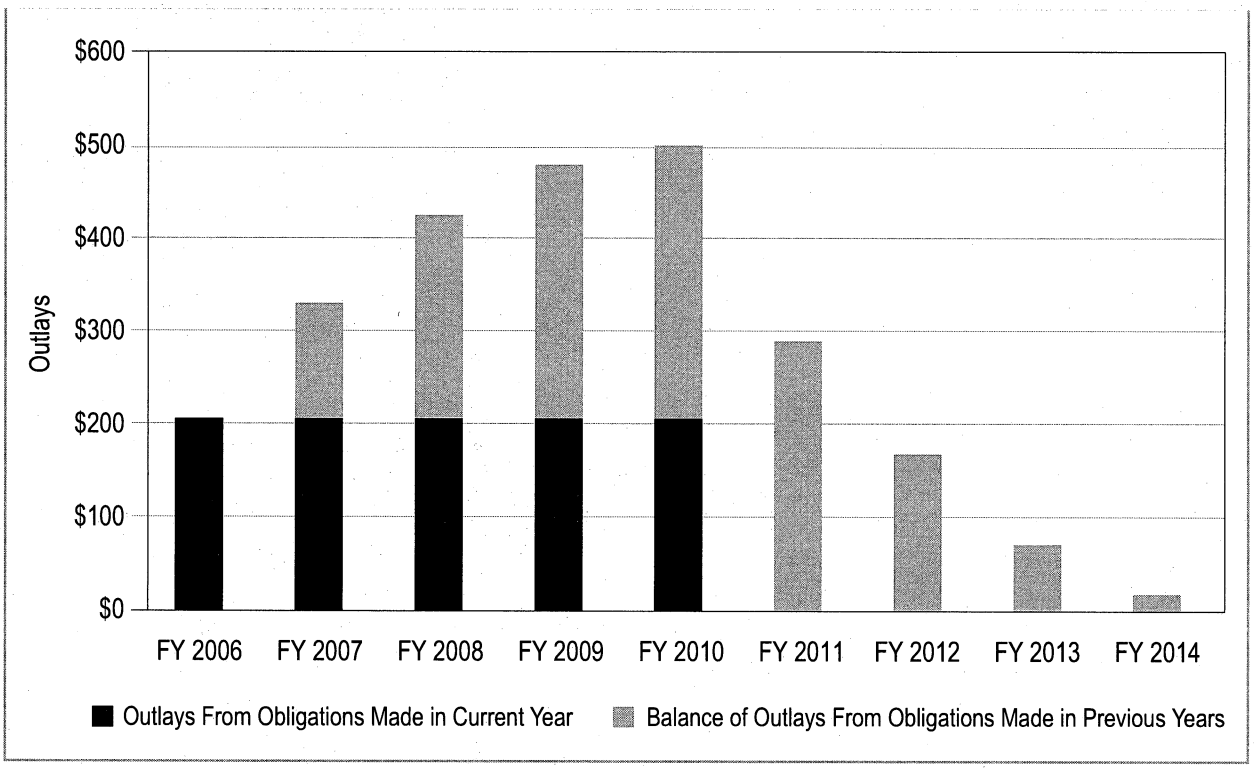


Figure 5-2. Cash Flow by Fiscal Year for the National Advanced Technology Initiative for Cancer (dollars in millions)

Summary of Overall Base Level Funding to State/Regional Technology Hubs and Specialized Technology Nodes: Table 5-6 shows the projected funding for the hubs and nodes. Hubs will be funded through a combination of technology and Other Transactions Authorities granted to fund these consortia (which are unprecedented in their scope for the cancer research enterprise). To date, the best example of these types of consortia are funded and managed through the National Aeronautics and Space Administration to achieve their advanced technology goals. A small number of specialized technology nodes will be funded though a technology research grants program to allow investigators in academic institutions to develop cutting-edge technologies and to join major hubs when the timing is appropriate. At maturity, the NATIc will comprise 10 hubs, which will engage 50 institutions and other technology development entities.

Table 5-6. NATIc Advanced Technology Hubs and Specialized Technology Nodes Summary Points (dollars in millions)

State/Regional Advanced Technology Hubs	
Total Number of State/Regional Advanced Technology Hubs	**10**
Total Number of Participating Entities	**50**
Number of Institutions for Each State/Regional Advanced Technology Hub	**5**
Total Program Funds	**$1,280**
Total Funds to Each State/Regional Advanced Technology Hub	**$128**
Total Funds to Each Entity	**$26**
Specialized Technology Nodes	
Total Number of Specialized Technology Nodes	**5**
Total Number of Participating Entities	**10**
Number of Institutions for Each Specialized Technology Node	**2**
Total Program Funds	**$40**
Total Funds to Each Specialized Technology Node	**$8**
Total Funds to Each Entity	**$4**

Summary: The funding model for the NATIc places emphasis on creating the advanced technology hubs as effectively and rapidly as possible to optimize their ability to develop partnerships. The increased flow of intellectual property from the NATIc will provide a major impetus for the development of public-private partnerships and new company formation that could become a major source of additional funding for the hubs. In fact, the technology development "pipelines" from these hubs could continue to mature for several years.

Additional Authority Needed to Implement the NATIc: The NATIc is an unprecedented concept in biomedicine, and it will require new resources, as well as innovative mechanisms, to achieve its goal of fueling the biomedical technology revolution that will enable reaching the NCI's goal of eliminating the suffering and death due to cancer in the next decade. The additional authority requested to implement the NATIc ia an expansion of the NCI's current authority to award grants, contracts, and cooperative agreements through **Other Transaction Authorities**.

Justification for Other Transactions Authority: To facilitate the support of the projects of the NATIc, other transactions authorities will be requested to streamline the procurement processes and facilitate the acquisition of materials and services to support the hubs, nodes, Strategic Technology Development Program, and technology grants. The NATIc technology development programs require sufficient flexibility and integration to enable the interactions among a wide array of institutions and organizations. In addition, because of the established timelines for the NATIc, expedited review procedures and workflow processing will be needed to conduct the procurement in sequence with the program needs. Other transactions may include direct solicitation from known laboratories or other sources of technology, and capability to terminate contracts at the convenience of the government. This authority will enable the assembly of teams of scientists and technologies to conduct directed research to create specifically designed technology platforms.

For many of the technology platforms to be created through this initiative, there will be significant need for coordination of the licensing and patenting activities among the grantees and contractors. A significant impediment for the entry of technologies into the health care marketplace is the cross-licensing required for multicomponent technology platforms. It is requested that an accelerated process for determination of exceptional circumstances (DEC) and deviated Federal Acquisition Regulations (FAR) clauses, when deemed valuable to the broad research enterprise, be implemented.

To support the timelines for the projects and the requirement for a high level of integration to be involved, additional mechanisms for peer review of scientific projects and proposals should be available. This involves the use of expert technical panels and scientific review committees to evaluate project proposals and project milestones as an alternative to existing scientific review processes.

Suggested Language for Authorizations: The following language is suggested for other transaction authorities for this initiative:

> *(a) Authority. Notwithstanding any other provision of the law, the Director of the National Cancer Institute may use funds available under section 402(i) of the Public Health Service Act [42 U.S.C. 282(i)] to enter into transactions (other than contracts, cooperative agreements, or grants) to carry out research in support of the National Advanced Technology Initiative for Cancer (NATIc). (b) Peer Review. In entering into transactions under subsection (a), the Director of the National Cancer Institute may utilize such peer review procedures (including consultation with appropriate scientific experts) as the Director determines to be appropriate to obtain such assessments of scientific and technical merit.(c) Applicability. Procedures shall apply to such transactions in lieu of the peer review and advisory council review procedures that would otherwise be required under sections 301(a)(3), 405(b)(1)(B), 405(b)(2), 406(a)(3)(A), 492, and 494 of the Public Health Service Act [42 U.S.C. 241, 284(b)(1)(B), 284(b)(2), 284a(a)(3)(A), 289a, and 289c].*

Authorities Available Under the FFRDC to Serve as the Coordinating Hub and Provide Contract Support for the State/Regional Technology Hubs: In developing the funding models for the State/regional technology hubs, one strategic mechanism for funding and program management is through the use of the DHHS Federally Funded Research and Development Center (FFRDC), known as NCI-Frederick, Frederick, Maryland. The FFRDC mechanism is used by many Federal agencies to operate laboratories through private contractors for large R&D projects. For example, the Department of Energy, National Aeronautics and Space Administration, and the Department of Defense use this management approach to operate mission-critical R&D operations. The FFRDC approach to managing laboratory operations through a private contractor, initially recommended by the National Academy of Sciences, allows the Federal Government certain flexibilities and efficiencies in acquisitions of goods and services, subcontracting capabilities, human resource management, and management of intellectual property that standard government contracting mechanisms do not allow.

Since 1972, the NCI has administered this FFRDC, which is operated by a primary Operations and Technical Support (OTS) contract. The FFRDC mechanism has been used by NCI to provide infrastructure to the research enterprise such as animal models, biospecimen repositories, biopharmaceutical scale-up, and natural products. In addition, the FFRDC has proven to be an effective and efficient means of managing some extramural subcontracted programs at universities and research centers for developing core resources in genomics, proteomics, and technology platforms.

The NATIc business plan proposes to use the FFRDC mechanism to fund and manage a portion of the contracts to support the Strategic Technology Development Program. In this plan, the FFRDC contractor would fund subcontracts to the institutions constituting the technology hubs. As is done for current projects, solicitations for proposals for specific technology projects would be made to the hubs and a rigorous review of the technical proposals would be conducted by project managers and contracting officers, and awards made on a competitive negotiated basis. The FFRDC contractor would award subcontracts to the institutions. Each step of these processes would be conducted in close consultation with experienced NCI program and contract staff to ensure oversight of this aspect of the program.

The DHHS FFRDC at NCI-Frederick is ideally suited for the flexible, integrated strategy needed to respond in a timely, effective, and efficient manner to this program to engineer the best technology platforms possible. In addition, the proposed use of the FFRDC, serving as one element of the funding models used for the NATIc, is consistent with the principles of the President's Management Agenda and will ensure that taxpayers' resources are used as effectively as possible.

Summary: The NATIc is a revolutionary concept to harness the highly sophisticated array of resources that have evolved from our Nation's commitment to biomedical research, the NIH Roadmap initiatives, and the regional/State capabilities in advanced technology development for biomedicine. Funded at $2.5 billion through a Federal, philanthropic, and private partnership, it will create an unprecedented virtual network of advanced technology hubs that will coordinate and leverage the resources of cancer and academic centers, State and regional centers of biotechnology and innovation, national laboratories, and other partners. This virtually connected network provides a revolutionary approach to developing the advanced biomedical technologies needed to achieve the NCI's goal of eliminating suffering and death due to cancer in a decade.

Chapter 6: Benefits to the Nation – Milestones and Metrics

Development of technology has the power to produce exponential progress against cancer and to improve people's lives. The NATIc will function as an integrated technology development and integration enterprise to create breakthrough health care technologies and make them available to all sectors. To accomplish specific cancer technology milestones, strategies for early detection, prevention, and prediction will be linked to key national resources such as validated tissue repositories, biomarkers of risk, and cancer genome and proteomic profiles. The NATIc will also integrate advances in physics and microchip technology with engineering and medicine.

Table 6-1 presents an integrated summary of the NATIc's management, administrative, and key technology milestones and deliverables by year and cumulative investment from FY 2006 to FY 2014.

As summarized in the table, the plan is to aggressively launch the NATIc by creating up to 8 of the anticipated 10 advanced technology hubs in FY 2006. The NCI-Frederick FFRDC Coordinating Center, NCI Program Management Group, and the NATIc's Senior Technical Council will be established in FY 2006. In fact, to achieve the rapid ramp-up of the program needed to establish the NATIC's advanced technology development hubs, all of the management functions and processes for the initiative will be established during the first year. The NCI also plans to implement the Strategic Technology Development Program through the FFRDC to allow the hubs to undertake the development of specific advanced diagnostics, therapeutic, and preventive cancer technologies.

The flow of technical milestones and deliverables over the life of the program begins with the integration of the hubs through a common bioinformatics platform and the deployment of certain key technology development platforms as follows:

- *The Cancer Bioinformatics Grid (caBIG).* Through the deployment of the NCI's caBIG, the NATIc will achieve the architecture, interoperability, and programs needed to support the NATIc's absolute requirement for connectivity and real-time data exchange in FY 2006, with further refinement in FY 2007. This milestone will ensure the connectivity and data exchange capability required by all of the hubs to fully deliver advanced technologies in FY 2006 and beyond.
- *National Biospecimen Resource.* The NATIc will establish a national (and international) biospecimen resource and associated database to ensure that data can be compared across its technology development hubs.

As hubs come online and adopt a common bioinformatics infrastructure, along with other broad technology platforms, the pace of technology development will speed up significantly. As illustrated in **Table 6-1**, due to the breadth and depth of the NATIc's virtual advanced technology development capacity, targeted cancer drugs and devices that today are years away can be achieved in months to a few years. The availability of nearly any expertise and advanced technology platform, along with scale-up and prototyping capabilities of the NATIc, will foster exponential progress. Moreover, the contract mechanisms employed for the competitive Strategic Technology Development Program will allow the NATIc to stop non-productive programs and move on to new technical challenges for the network. Some of the advanced technical development milestones expected in the mid to late years of the program are bold, but through this innovative concept, the NCI believes that they are achievable.

The final technical deliverables for the program in FY 2014 are summarized in the table. Although this list may seem unattainable, it is not. The potential is resident in what is now a fragmented enterprise with limited opportunity to leverage the enormous wave of investments in advanced technology development and innovation currently under way in States and regions across the Nation. Seizing this moment and creating the NATIc will transform our current fragmented system into a robust seamless system of technology development to conquer cancer and transform 21st century medicine.

Some outcomes of the NATIc that will underpin this transformation include:

- The NATIc hubs will systematically characterize the genetic changes involved in the initiation and development of all cancers. A national-scale "Human Cancer Genome Project" will drive rapid technology development and produce a "map" of all key genetic alternations for each cancer.

- The NATIC will characterize a set of biomarkers for every cancer.

- Through nanotechnology platforms, the NATIc will offer a new generation of diagnostics with the capability of diagnosing all abnormal proteins from a patient's single drop of blood.

- To revolutionize the diagnosis and treatment of cancer, the NATIc will develop and deploy targeted imaging agents, minimally invasive image-guided technologies, and advanced detectors.

- The NATIc network will produce a minimum of 20-25 targeted, safe, highly efficacious drugs for delivery to the right patients at the right time using biomarkers to ensure maintenance of the therapeutic response.

Table 6-1 summarizes the scope and magnitude of the health care technology returns that can be expected from investment in the NATIc. However, this list is only part of the story. The economic effects of the advanced biomedical technologies that will come from this paradigm-shifting initiative will have impact far beyond the hubs and nodes that comprise the NATIc.

NATIc investments will drive the development and commercialization of advanced technologies that are critical to transforming cancer diagnosis, treatment, and prevention. Currently, there are approximately 1,500 biotechnology companies in the United States, which provide more than 150,000 advanced technology jobs and support another 290,000 positions in service to the industry.[1] The increased flow of advanced biomedical technologies from the NATIc has the potential to significantly increase the formation of new biotechnology companies. Licensing revenues and royalty streams to cancer and academic medical centers would also be expected to increase significantly. Given NATIc's technology development investment strategy, the economic development effects on advanced technology job creation could be significant in States and regions that have invested to support advanced biomedical "clusters" such as California, Florida, Georgia, Maryland, Massachusetts, Michigan, North Carolina, Ohio, Pennsylvania, Wisconsin, and others.

One of the key outcomes of the NATIc will be new models for effective partnerships. It is anticipated that State and regional technology innovation centers will participate in the NATIc and that each of the hubs will have an active technology transfer program to fuel the development of biotechnology companies. Partnerships with other Federal agencies as exemplified by the NCI/FDA Oncology Task Force and the National Cancer Institute-Centers for Medicare and Medicaid Services Task Force will also be a critical part of the NATIc's strategy to accelerate the rate of technology development and commercialization.

Finally, as we attempt to estimate the returns on the proposed investment in the NATIc, it is critical to keep in mind that the biggest returns will come from the early diagnosis, prevention, and targeted treatment of all cancers. The vision of the NCI is to eliminate the suffering and death due to cancer, which would save more than 560,000 lives per year in the United States alone and eliminate one of the biggest public health problems that America faces in the next two decades. Of greater importance, countless numbers of years of high-quality life will be restored to patients and they will live with cancer as a chronic, non-lethal disease. Overall, the returns from our investment in the NATIc will provide a critical and required strategic element to achieve the NCI's goal of eliminating suffering and death due to cancer in a decade and will have a real-time impact on the health of all Americans.

[1]The Economic Contributions of the Biotechnology Industry to the U.S. Economy. Ernst & Young, 2000

Table 6-1. NATIc Milestones and Deliverables for FY 2006 - FY 2014 (dollars in millions)			
Fiscal Year	**Administrative and Management Milestones**	**Advanced Technology Development Milestones**	**Budget Outlays**
2006	Set Up Administrative and Program Management System Establish NATIc Senior Technical Council – Initiate Quarterly Hub Reviews Competition, Award of Contracts and Obligation of Funds and Begin Outlays Establish Central Coordinating Center at the FFRDC and Initiate Services and Cross-Hub Common Technology Distribution Establish up to 8 Advanced Technology Hubs Launch Strategic Development Program Through Existing Hubs – With 5-6 Programs Approved – and Outlays Initiated Initiate Monitoring of Strategic Technology Development Program Through Milestone Achievement Annual Program Evaluation	• Establish up to 8 hubs in year 1 from the following areas: advanced imaging, drug discovery and high-throughput screening; proteomics, biomarkers and diagnostics; computational and systems biology; nanotechnology; high-throughput genomics sequencing; biopharmaceutical development and scale-up; biosensors and model systems engineering; bioengineering and advanced prototyping • Initiate NATIc Cancer Bioinformatics Grid (caBIG) integration in all hubs • Pilot program for sequencing human cancer genes initiated through selected hubs • All major NCI-supported databases identified and begin deployment to hubs through caBIG • Common materials and technologies to support biomarkers development made broadly available to hubs • High-throughput screens set up and screening initiated at selected hubs • Common national biospecimen resource pilot initiated at all hubs to support discovery and development • Plan to coordinate/develop pharmaceutical scale-up for network	**$206**
		Total Outlays in 2006	**$206**
2007	Competition to Select Additional Advanced Technology Hubs Select Additional Hubs – for a Total of 10 Funded Consortia Initiate Technology Grants Program – Select up to 3 Specialized Technology Nodes Outlays to Approximately 50 Participating Entities Increase Numbers of Programs Through Strategic Technology Development Program, 5-6 Additional Awards Distribute and Coordinate Selected Cross-Hub Common Platform Technologies Milestone Evaluations of All Hubs and Strategic Technology Development Contract Programs Annual Program Evaluation	• Additional hubs established to achieve total of up to 10 in areas defined for 2006 and initiate formation of nodes • Complete deployment of caBIG to all hubs and connect to cancer enterprise • Begin national high-throughput screening to identify up to 100 lead candidate molecules for cancer therapy and prevention/year • Develop and deploy "Smartcard" for clinical trials to support evaluation of targeted agents • Establish national hub scale-up capabilities for new targeted chemopreventive and therapeutic agents • Set up national system to identify and validate proteomic biomarkers for breast, prostate, lung, and colon cancers • Deployment of the first generation nanotechnology-based diagnostics platform to measure up to 1,000 biomarkers for 2 or more cancer types • Establish network to identify all pathways in cancer cell through systems biology – computational model • Offer full device prototyping capabilities to hubs	**$332**
		Cumulative Outlays	**$538**
2008	Evaluate Hubs, Based on Milestones, Re-compete and Award New Hubs as Appropriate Award Additional Nodes as Approved Through Technology Grants Program Award 4-5 New Initiatives Through Strategic Technology Development Program Continue All Milestone Evaluations of Hubs and Contracts for Specific Technologies and Platforms Redistribute Funds as Appropriate Based on Milestone Evaluations Overall Interim Program Evaluation and Report Out	• New generation of microchips to measure to provide high-throughput capability to measure all genetic changes in cancer cells • Deploy first-generation proteomics-based diagnostic device(s) to measure specific proteins in blood • New integrated clinical trials system to evaluate targeted agents in 3 years or less – and bring to market in 5 years or less • Begin robotics-based national high-throughput screening to identify up to 500 lead candidate molecules for cancer therapy and prevention/year • Deliver a system to develop new targeted contrast agents for advanced imaging – 2-3 reaching the market/year • Integrate systems for gene expression sensing response for molecular therapy into 10 clinical trials for solid tumors • Deliver first platform construct for multicomponent chemoprevention strategy that incorporates safety monitoring through biosensing devices • Demonstrate the first drugs-screening platform that integrates chemistry, nanotechnology, biophysics, informatics, and high-throughput assay system	**$427**
		Cumulative Outlays	**$965**

2009	Evaluate Hubs, Based on Milestones, Re-compete and Award New Hubs as Appropriate Continue Technology Grants Program, With New Nodes as Approved Award 4-5 New Initiatives Through Strategic Technology Development Program Evaluate all Ongoing Strategic Technology Development Programs Based on Milestones – Re-deploy Funds as Appropriate Receive Completed Prototypes and Submissions From Projects Completed Through the Strategic Technology Development Program Annual Program Evaluation	• Establish first remote reprogrammable multicomponent nanodelivery devices for clinical testing • Integrate new optical imaging device for dynamic assessment of subcellular protein trafficking • Implement common nanotechnology platform for guided laser ablation of solid tumor at resolution of <1,000 cells • Deploy remote data sensing device for detection of metastatic cells as standard clinical monitoring tool for assessing state of disease • Integrate national drug screening platform that integrates chemistry, nanotechnology, informatics and high-throughput assays into national cancer drug development program • Implement first stage of 'virtual" cancer management model – using online data recordings of sensing devices for proteins and genes • Deliver the first clinical model of "whole genome" scans of genetic mutations and expression levels as risk determinant methods for cancer detection/screening	**$481**
			Cumulative Outlays **$1,446**
2010	Award New Hubs Based on Funds Becoming Available Due to Re-deployment Milestones Evaluation Continue Technology Grants Program, With New Nodes as Approved Award 3-4 New Initiatives Through Strategic Technology Development Program Evaluate All Ongoing Strategic Technology Development Programs Based on Milestones – Re-deploy Funds as Appropriate Receive Completed Prototypes and Submissions From Projects Completed Through the Strategic Technology Development Program Begin Transitioning Hubs through Private/Philanthropic/Venture Partnerships and Funds Annual Program Review	• Complete nationwide, virtually connected, privacy-protected, biospecimen resource and bioinformatics database • "Catalogue" of all cancer genetic abnormalities for major cancers with progress on rare cancers • Deploy advanced molecular imaging platforms to visualize functional changes in cancers • A minimum of 20 new targeted therapeutic drugs for cancer in trials – 6-8 or more entering the market/year • A minimum of 6 new genetically targeted chemopreventive drugs in clinical trials with 3-4 entering the market/year • Define new cancer molecular targets through computer-assisted devices use of integrated maps of cancer cell control systems	**$502**
			Cumulative Outlays **$1,948**
2011	Continue Technology Grants Program, With New Nodes as Approved Evaluate All Ongoing Strategic Technology Development Programs Based on Milestones – Re-deploy Funds as Appropriate Receive Completed Prototypes and Submissions From Projects Completed Through the Strategic Technology Development Program Continue Hub Milestone Evaluations – Redeploy Any New Funds Among Existing Hubs Transitioning of Hubs Through Acquisition of Private/Philanthropic/Venture Partnerships and Funds Annual Program Review	• A minimum of 40 new targeted therapeutic drugs for cancer in trials – 10 or more entering the market • A minimum of 10-20 new targeted chemopreventive drugs for cancer in trials, 8 or more entering the market • Deploy implantable nanotechnology biosensor to detect genetic changes in risk populations in real time • General use of functional imaging platform for tumors to show real-time changes, drug delivery and targets • Define new targets for early detection using 3-dimensional computer models of molecular interactions • Release first-generation blood/serum biomarker diagnostic platform(s)	**$292**
			Cumulative Outlays **$2,240**

2012	Evaluate all Ongoing Strategic Technology Development Programs Based on Milestones – Re-deploy Funds as Appropriate Receive Completed Prototypes and Submissions From Projects Completed Through the Strategic Technology Development Program Continue Technology Grants Program, With New Nodes as Approved Continue Transitioning of Hubs Through Acquisition of Private/Philanthropic/Venture Partnerships and Funds Annual Program Review	• Complete comprehensive set of biomarkers to define the identity of each cancer early in its development • A minimum of 50 new genetically targeted therapeutic drugs for cancer in trials – with 20 new drugs entering the market • A minimum of 15 new genetically targeted chemopreventive drugs in trials with 10 entering the market • General deployment of a nanotechnology – microfluidics-based diagnostics platform to diagnose all cancers using a minimum of 1000 biomarkers	**$169**
		Cumulative Outlays	**$2,409**
		NATIc Final Deliverables	
2013-2015	Receive Completed Prototypes and Submissions From Projects Completed Through the Strategic Technology Development Program Evaluate all Ongoing Strategic Technology Development Programs Based on Milestones Finalize Transitioning of Hubs Through Acquisition of Private/Philanthropic/Venture Partnerships and Funds Continue Level of NCI Operations Funding if Needed – Not to Exceed $75-100 M/Year through 2015 Final Program Review	• National biospecimen resource to support all post-genomic research • Cancer bioinformatics network that connects all scientists, clinicians, and components of the cancer research and health delivery enterprise • Catalogue of every genetic abnormality that serves as a basis for all types of cancers • Comprehensive set of protein biomarkers that identify every type of cancer • Fifty new targeted drugs for cancer treatment and/or preventives in clinical trials with 20-25 entering the marketplace • Diagnostic nanotechnology and other platforms to identify all significant abnormal proteins in a drop of blood • A seamless system of drug development, including clinical trials that require 5 years or less from lead compound identification to regulatory approval • "Smartcard" supported clinical trials system to create transparent, patient-friendly trials connected to electronic-medical records • Systems biology understanding of all the abnormal pathways in cancer cells to support cancer prevention, early detection and treatment • Functional molecular imaging platforms to diagnose cancer, guide therapeutic delivery, and monitor treatment response	**$91**
		Cumulative Outlays	**$2,500**

Appendix A

Table A-1. Crosswalk of Obligations by Function to Funding Source - FY 2006 - FY 2010
(dollars in millions)

	Total for Program 2006-2010				2006				
Advanced Technology Hubs and Specialized Technology Nodes:	NATIc Approp	Philanthropy	NCI Approp	Total	#	NATIc Approp	Philanthropy	NCI Approp	Total
State/Regional Advanced Technology Hubs	$1,280			$1,280	8	$205			$205
{Participating Entities}					{40}				
Specialized Technology Nodes		$10	$30	40					
{Participating Entities}									
National Coordinating Center at NCI-Frederick			100	100	1			$20	20
Subtotal Hubs and Nodes	1,280	10	130	1,420		205		20	225
Strategic Technology Development Program	220	490	319	1,029		95	$100	71	266
Management and Support			51	51				9	9
Total Obligations	1,500	500	500	2,500		300	100	100	500

	2007					2008				
Advanced Technology Hubs and Specialized Technology Nodes:	#	NATIc Approp	Philanthropy	NCI Approp	Total	#	NATIc Approp	Philanthropy	NCI Approp	Total
State/Regional Advanced Technology Hubs	10	$268			$268	10	$269			$269
{Participating Entities}	{50}					{50}				
Specialized Technology Nodes	5		$10		10	5			$10	10
{Participating Entities}	{10}					{10}				
National Coordinating Center at NCI-Frederick	1			$20	20	1			20	20
Subtotal Hubs and Nodes		268	10	20	298		269		30	299
Strategic Technology Development Program		32	90	69	191		31	$100	59	190
Management and Support				11	11				11	11
Total Obligations		300	100	100	500		300	100	100	500

	2009					2010				
Advanced Technology Hubs and Specialized Technology Nodes:	#	NATIc Approp	Philanthropy	NCI Approp	Total	#	NATIc Approp	Philanthropy	NCI Approp	Total
State/Regional Advanced Technology Hubs	10	$269			$269	10	$269			$269
{Participating Entities}	{50}					{50}				
Specialized Technology Nodes	5			$10	10	5			$10	$10
{Participating Entities}	{10}					{10}				
National Coordinating Center at NCI-Frederick	1			20	20	1			20	20
Subtotal Hubs and Nodes		269		30	299		269		30	299
Strategic Technology Development Program		31	$100	60	191		31	$100	60	191
Management and Support				10	10				10	10
Total Obligations		300	100	100	500		300	100	100	500

Appendix B

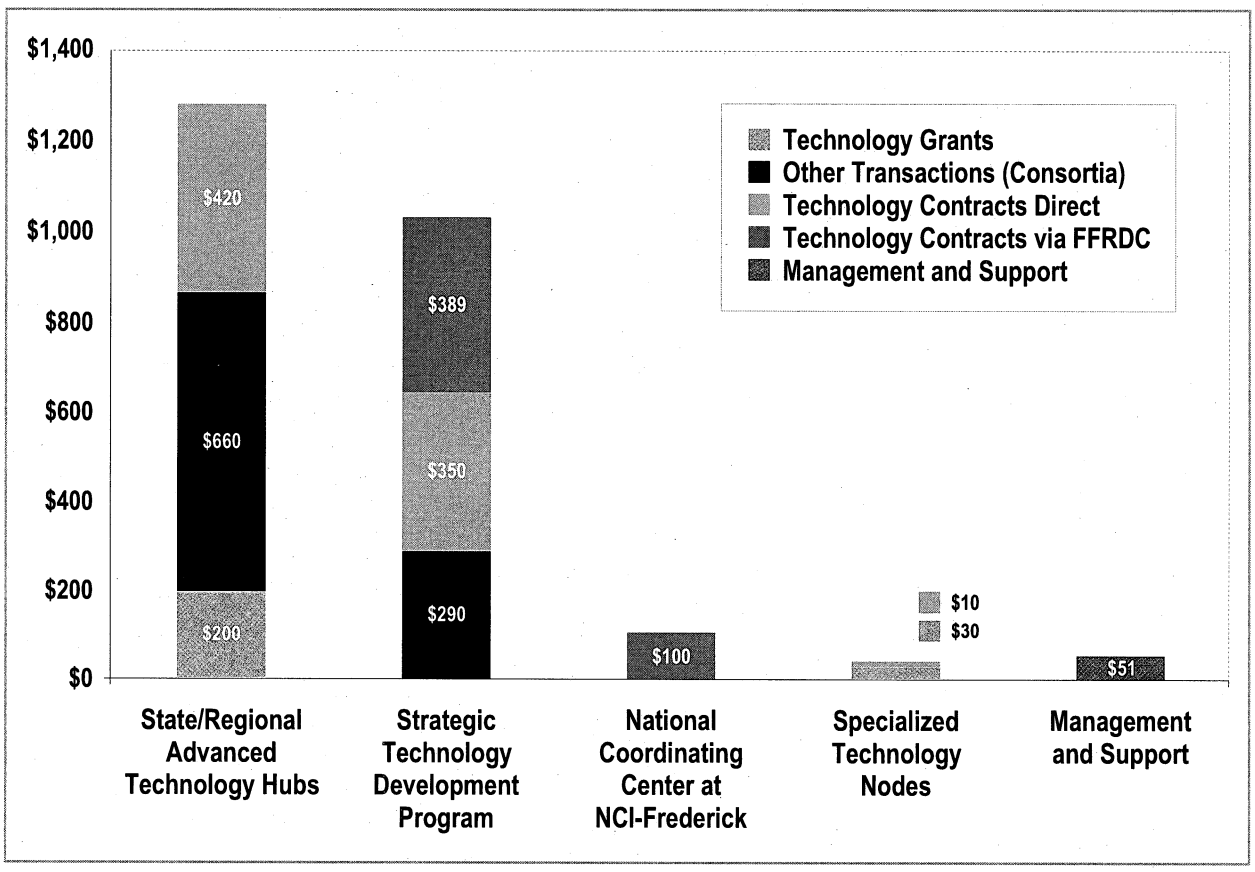


Figure B-1. Funding by Function and Mechanism for the National Advanced Technology Initiative for Cancer (dollars in millions)

Appendix C

Table C-1. Total Outlays (Obligations from all Funding Sources) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$500	$500	$500	$500	$500	$0	$0	$0	$0	$2,500
	Obligations										
FY 2006											
From Current Year Obligations	$500	206	124	97	53	20					
From Prior Year Obligations											
Total		206	124	97	53	20					
FY 2007											
From Current Year Obligations	$500		208	122	97	53	20				
From Prior Year Obligations			124	97	53	20	0				
Total			332	219	150	73	20				
FY 2008											
From Current Year Obligations	$500			209	123	97	52	19			
From Prior Year Obligations				218	150	74	20	0			
Total				427	273	171	72	19			
FY 2009											
From Current Year Obligations	$500				208	123	97	53	19		
From Prior Year Obligations					273	171	72	19	0		
Total					481	294	169	72	19		
FY 2010											
From Current Year Obligations	$500					208	123	97	53	19	
From Prior Year Obligations						294	169	72	19	0	
Total						502	292	169	72	19	
Grand Total Outlays from all Sources		**$206**	**$332**	**$427**	**$481**	**$502**	**$292**	**$169**	**$72**	**$19**	**$2,500**

Appendix D

Table D-1. Total Outlays by Funding Source (Obligations from NATIc Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$300	$300	$300	$300	$300	$0	$0	$0	$0	$1,500
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$300	121	75	60	32	12					
From Prior Year Obligations											
Total		121	75	60	32	12					
FY 2007											
From Current Year Obligations	$300		121	75	60	32	12				
From Prior Year Obligations			75	60	32	12	0				
Total			196	135	92	44	12				
FY 2008											
From Current Year Obligations	$300			121	75	60	32	12			
From Prior Year Obligations				134	92	45	12	0			
Total				255	167	105	44	12			
FY 2009											
From Current Year Obligations	$300				121	75	60	32	12		
From Prior Year Obligations					167	105	44	12	0		
Total					288	180	104	44	12		
FY 2010											
From Current Year Obligations	$300					121	75	60	32	12	
From Prior Year Obligations						180	104	44	12	0	
Total						301	179	104	44	12	
Total Outlays from NATIc Appropriation		**121**	**196**	**255**	**288**	**301**	**179**	**104**	**44**	**12**	**1,500**

Table D-2. Total Outlays by Funding Source (Obligations from NCI Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$100	$100	$100	$100	$100	$0	$0	$0	$0	$500
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$100	45	24	17	10	4					
From Prior Year Obligations											
Total		45	24	17	10	4					
FY 2007											
From Current Year Obligations	$100		47	22	17	10	4				
From Prior Year Obligations			24	17	10	4	0				
Total			71	39	27	14	4				
FY 2008											
From Current Year Obligations	$100			48	23	17	9	3			
From Prior Year Obligations				39	27	14	4	0			
Total				87	50	31	13	3			
FY 2009											
From Current Year Obligations	$100				47	23	17	10	3		
From Prior Year Obligations					50	31	13	3	0		
Total					97	54	30	13	3		
FY 2010											
From Current Year Obligations	$100					47	23	17	10	3	
From Prior Year Obligations						54	30	13	3	0	
Total						101	53	30	13	3	
Total Outlays from NCI Appropriation		**45**	**71**	**87**	**97**	**101**	**53**	**30**	**13**	**3**	**500**

Table D-3. Total Outlays by Funding Source (Obligations from Philanthropy) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$100	$100	$100	$100	$100	$0	$0	$0	$0	$500
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$100	40	25	20	11	4					
From Prior Year Obligations											
Total		40	25	20	11	4					
FY 2007											
From Current Year Obligations	$100		40	25	20	11	4				
From Prior Year Obligations			25	20	11	4	0				
Total			65	45	31	15	4				
FY 2008											
From Current Year Obligations	$100			40	25	20	11	4			
From Prior Year Obligations				45	31	15	4	0			
Total				85	56	35	15	4			
FY 2009											
From Current Year Obligations	$100				40	25	20	11	4		
From Prior Year Obligations					56	35	15	4	0		
Total					96	60	35	15	4		
FY 2010											
From Current Year Obligations	$100					40	25	20	11	4	
From Prior Year Obligations						60	35	15	4	0	
Total						100	60	35	15	4	
Total Outlays from Philanthropy		**40**	**65**	**85**	**96**	**100**	**60**	**35**	**15**	**4**	**500**

Appendix E

Table E-1. State/Regional Advanced Technology Hubs
(Obligations from NATIc Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$205	$268	$269	$269	$269	$0	$0	$0	$0	$1,280
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$205	83	51	41	22	8					
From Prior Year Obligations											
Total		83	51	41	22	8					
FY 2007											
From Current Year Obligations	$268		108	66	54	29	11				
From Prior Year Obligations			51	41	22	8	0				
Total			159	107	76	37	11				
FY 2008											
From Current Year Obligations	$269			108	67	54	29	11			
From Prior Year Obligations				107	76	37	11	0			
Total				215	143	91	40	11			
FY 2009											
From Current Year Obligations	$269				108	67	54	29	11		
From Prior Year Obligations					143	91	40	11	0		
Total					251	158	94	40	11		
FY 2010											
From Current Year Obligations	$269					108	67	54	29	11	
From Prior Year Obligations						158	94	40	11	0	
Total						266	161	94	40	11	
Total Outlays from NATIc Appropriation		**83**	**159**	**215**	**251**	**266**	**161**	**94**	**40**	**11**	**1,280**

Appendix F

Table F-1. Strategic Technology Development Program
(Obligations from NATIc Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$95	$32	$31	$31	$31	$0	$0	$0	$0	$220
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$95	38	24	19	10	4					
From Prior Year Obligations											
Total		38	24	19	10	4					
FY 2007											
From Current Year Obligations	$32		13	8	6	4	1				
From Prior Year Obligations			24	19	10	4	0				
Total			37	27	16	8	1				
FY 2008											
From Current Year Obligations	$31			13	8	6	3	1			
From Prior Year Obligations				27	16	8	1	0			
Total				40	24	14	4	1			
FY 2009											
From Current Year Obligations	$31				13	8	6	3	1		
From Prior Year Obligations					24	14	4	1	0		
Total					37	22	10	4	1		
FY 2010											
From Current Year Obligations	$31					13	8	6	3	1	
From Prior Year Obligations						22	10	4	1	0	
Total						35	18	10	4	1	
Total Outlays from NATIc Appropriation		**38**	**37**	**40**	**37**	**35**	**18**	**10**	**4**	**1**	**220**

Table F-2. Strategic Technology Development Program (Obligations from NCI Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$71	$69	$59	$60	$60	$0	$0	$0	$0	$319
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$71	28	18	14	8	3					
From Prior Year Obligations											
Total		28	18	14	8	3					
FY 2007											
From Current Year Obligations	$69		28	16	14	8	3				
From Prior Year Obligations			18	14	8	3	0				
Total			46	30	22	11	3				
FY 2008											
From Current Year Obligations	$59			25	14	12	6	2			
From Prior Year Obligations				30	22	11	3	0			
Total				55	36	23	9	2			
FY 2009											
From Current Year Obligations	$60				25	14	12	7	2		
From Prior Year Obligations					36	23	9	2	0		
Total					61	37	21	9	2		
FY 2010											
From Current Year Obligations	$60					25	14	12	7	2	
From Prior Year Obligations						37	21	9	2	0	
Total						62	35	21	9	2	
Total Outlays from NCI Appropriation		**28**	**46**	**55**	**61**	**62**	**35**	**21**	**9**	**2**	**319**

Table F-3. Strategic Technology Development Program (Obligations from Philanthropy) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$100	$90	$100	$100	$100	$0	$0	$0	$0	$490
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$100	40	25	20	11	4					
From Prior Year Obligations											
Total		40	25	20	11	4					
FY 2007											
From Current Year Obligations	$90		36	22	18	10	4				
From Prior Year Obligations			25	20	11	4	0				
Total			61	42	29	14	4				
FY 2008											
From Current Year Obligations	$100			40	25	20	11	4			
From Prior Year Obligations				42	29	14	4	0			
Total				82	54	34	15	4			
FY 2009											
From Current Year Obligations	$100				40	25	20	11	4		
From Prior Year Obligations					54	34	15	4	0		
Total					94	59	35	15	4		
FY 2010											
From Current Year Obligations	$100					40	25	20	11	4	
From Prior Year Obligations						59	35	15	4	0	
Total						99	60	35	15	4	
Total Outlays from Philanthropy		**40**	**61**	**82**	**94**	**99**	**60**	**35**	**15**	**4**	**490**

Appendix G

Table G-1. Specialized Technology Nodes (Obligations from NCI Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$0	$0	$10	$10	$10	$0	$0	$0	$0	$30
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$0	0	0	0	0	0					
From Prior Year Obligations											
Total		0	0	0	0	0					
FY 2007											
From Current Year Obligations	$0		0	0	0	0	0				
From Prior Year Obligations			0	0	0	0	0				
Total			0	0	0	0	0				
FY 2008											
From Current Year Obligations	$10			4	3	2	1	0			
From Prior Year Obligations				0	0	0	0	0			
Total				4	3	2	1	0			
FY 2009											
From Current Year Obligations	$10				4	3	2	1	0		
From Prior Year Obligations					3	2	1	0	0		
Total					7	5	3	1	0		
FY 2010											
From Current Year Obligations	$10					4	3	2	1	0	
From Prior Year Obligations						5	3	1	0	0	
Total						9	6	3	1	0	
Total Outlays from NCI Appropriation		**0**	**0**	**4**	**7**	**9**	**6**	**3**	**1**	**0**	**30**

Table G-2. Specialized Technology Nodes (Obligations from Philanthropy) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$0	$10	$0	$0	$0	$0	$0	$0	$0	$10
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$0	0	0	0	0	0					
From Prior Year Obligations											
Total		0	0	0	0	0					
FY 2007											
From Current Year Obligations	$10		4	3	2	1	0				
From Prior Year Obligations			0	0	0	0	0				
Total			4	3	2	1	0				
FY 2008											
From Current Year Obligations	$0			0	0	0	0	0			
From Prior Year Obligations				3	2	1	0	0			
Total				3	2	1	0	0			
FY 2009											
From Current Year Obligations	$0				0	0	0	0	0		
From Prior Year Obligations					2	1	0	0	0		
Total					2	1	0	0	0		
FY 2010											
From Current Year Obligations	$0					0	0	0	0	0	
From Prior Year Obligations						1	0	0	0	0	
Total						1	0	0	0	0	
Total Outlays from Philanthropy		**0**	**4**	**3**	**2**	**1**	**0**	**0**	**0**	**0**	**10**

Appendix H

Table H-1. National Coordinating Center at NCI-Frederick
(Obligations from NCI Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$20	$20	$20	$20	$20	$0	$0	$0	$0	$100
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$20	9	5	3	2	1					
From Prior Year Obligations											
Total		9	5	3	2	1					
FY 2007											
From Current Year Obligations	$20		9	5	3	2	1				
From Prior Year Obligations			5	3	2	1	0				
Total			14	8	5	3	1				
FY 2008											
From Current Year Obligations	$20			9	5	3	2	1			
From Prior Year Obligations				8	5	3	1	0			
Total				17	10	6	3	1			
FY 2009											
From Current Year Obligations	$20				9	5	3	2	1		
From Prior Year Obligations					10	6	3	1	0		
Total					19	11	6	3	1		
FY 2010											
From Current Year Obligations	$20					9	5	3	2	1	
From Prior Year Obligations						11	6	3	1	0	
Total						20	11	6	3	1	
Total Outlays from NCI Appropriation		**9**	**14**	**17**	**19**	**20**	**11**	**6**	**3**	**1**	**100**

Appendix I

Table I-1. Management and Support (Obligations from NCI Appropriation) (dollars in millions)

		FY2006	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	Total Obs
Extramural Operations		$9	$11	$11	$10	$10	$0	$0	$0	$0	$51
Outlays:											
	Obligations										
FY 2006											
From Current Year Obligations	$9	8	1	0	0	0					
From Prior Year Obligations											
Total		8	1	0	0	0					
FY 2007											
From Current Year Obligations	$11		10	1	0	0	0				
From Prior Year Obligations			1	0	0	0	0				
Total			11	1	0	0	0				
FY 2008											
From Current Year Obligations	$11			10	1	0	0	0			
From Prior Year Obligations				1	0	0	0	0			
Total				11	1	0	0	0			
FY 2009											
From Current Year Obligations	$10				9	1	0	0	0		
From Prior Year Obligations					1	0	0	0	0		
Total					10	1	0	0	0		
FY 2010											
From Current Year Obligations	$10					9	1	0	0	0	
From Prior Year Obligations						1	0	0	0	0	
Total						10	1	0	0	0	
Total Outlays from NCI Appropriation		**8**	**11**	**11**	**10**	**10**	**1**	**0**	**0**	**0**	**51**





NATIONAL® CANCER INSTITUTE

Eliminating the Suffering and Death DUE TO CANCER

Challenge goal 2015 – an overview

One American dies every minute as a result of cancer. Despite this grim statistic, it is clear that our medical and scientific communities are making tremendous progress. Three decades ago, there were 3 million cancer survivors in the United States; today, there are nearly 10 million. Death rates from the four most common cancers—lung, breast, prostate, and colorectal—continue to decline, indicating that our nation's investment in cancer research is paying dividends. The most significant benefit of that commitment, however, is about to be realized.

Over the past three decades, our struggle to cure cancer in the patient has been paralleled by our quest to understand cancer in the laboratory. Now we are poised to capitalize on the outputs of that *Discovery* process and *Develop* more effective interventions that, when *Delivered* to patients, will preempt the cancer process and eliminate a fatal outcome. Indeed, we are poised to eliminate the suffering and death due to cancer, and the NCI has committed to making this goal possible for all Americans by the year 2015.

This is a bold and visionary challenge. But it is one befitting the greatness of America. It is based on a rationale firmly rooted in the explosive pace of progress spawned by our robust biomedical research enterprise—an enterprise in which cancer researchers have consistently been at the forefront. NCI has led the effort over the past three decades to put into place the research and clinical programs required to effectively fight this disease. During this time, a national network of cancer centers has been established; an unsurpassed and robust basic and clinical research enterprise has been developed; and the cancer community has amassed a remarkable understanding of the mechanisms by which cancer develops and eventually progresses to its lethal state.

As a result of our continued commitment and understanding, we are now poised to exploit new opportunities to prevent many more cases of cancer; detect cancer at its earliest state; and, once cancer has been diagnosed, attack the disease at its weakest points and either eliminate it completely or keep it in check, much as we do with many chronic diseases. We will also maintain our commitment to applying research findings in the area of cancer control and population sciences to elucidate the role that behavioral, lifestyle, genetic, and environmental factors play in cancer initiation and progression.

To succeed, we must continue to drive the engine of discovery, fueled by fundamental research. Although our knowledge of cancer has expanded tremendously, we must learn more. So we have renewed our commitment to making new discoveries about cancer's genetic, molecular, and cellular puzzle. These discoveries are being translated into the development of new interventions—interventions that are designed for detection, diagnosis, and prediction, as well as treatment and prevention. Finally, once we develop these interventions, we will do what is necessary to ensure that they reach all who are in need.

Today, NCI continues to use the resources available to us as wisely and efficiently as possible. We have provided the leadership that has made the 2015 goal achievable, and we are defining the strategies necessary to achieve it and directing the tactics to make it a reality. Below are just a few of the initiatives and strategies that we believe are critical to meeting the 2015 goal.

Initiatives that take advantage of advanced technology…

- ***The Cancer Biomarker Project*** is identifying protein patterns and other molecular changes in saliva, sera, urine, or biopsy tissue that indicate the presence of a precancerous lesion or malignant tumor.
- ***The Advanced Cancer Imaging Project*** is moving us beyond anatomical to "next-phase" imaging methods that can more effectively detect and monitor cancer inside the body.
- ***The Cancer Nanotechnology Project*** will add a battery of agents and devices that function at the atomic and molecular levels, allowing for real-time monitoring of genetic and other changes associated with cancer.
- ***The Cancer Genome Project*** will allow researchers to systematically characterize the genes involved in nearly all forms of cancer.
- ***The Cancer Biomedical Informatics Grid*** will provide the critical informatics infrastructure that, for the first time ever, will connect teams of cancer and biomedical researchers from across the country, enabling them to share cutting-edge tools and data and vastly enhancing their ability to make rapid discoveries.

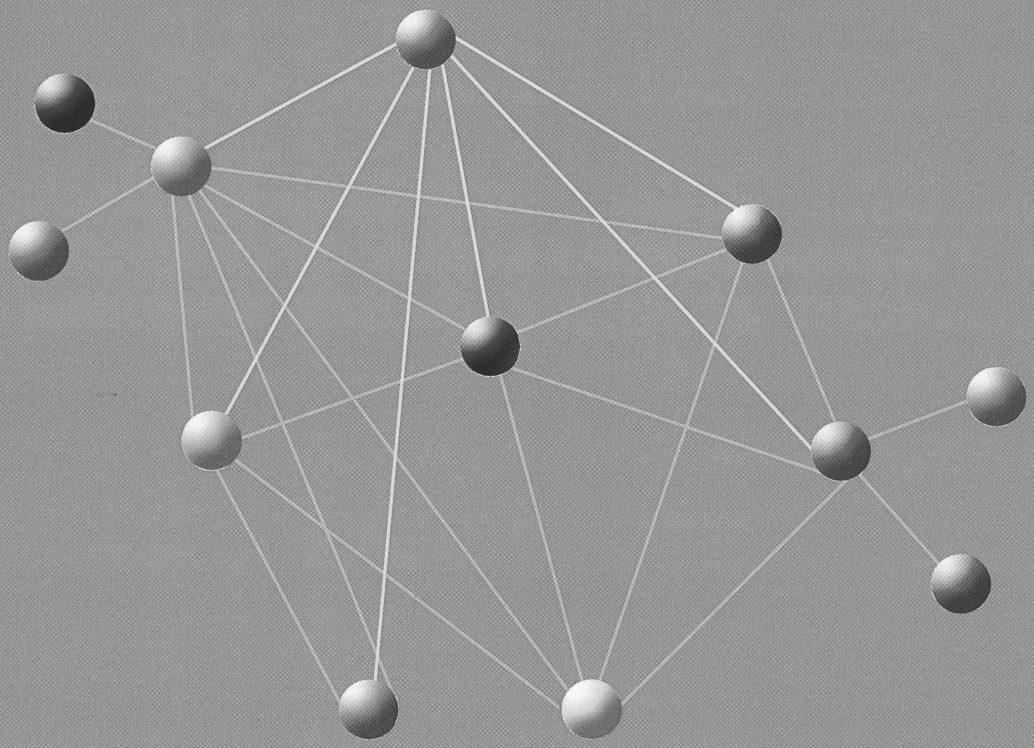
… Are leading to more effective cancer prevention, detection, control, and treatment strategies:

- ***Early Detection of Cancer*** – Novel approaches are being developed to prevent or intervene in the process of cancer development as well as more effectively treat the disease.
- ***Molecular Diagnosis*** – Clinicians will move beyond simply reacting to patient symptoms, instead performing molecular profiling and detection aimed at preempting cancer at the earliest possible stages.
- ***Molecularly Targeted Therapies*** – We are identifying genes and p roteins that contribute to cancer development and progression and translating these discoveries into validated "targets" for new therapies.
- ***Combination Therapies*** – We are moving toward strategically combining chemotherapeutic agents, radiation therapy, targeted molecular interventions, biologic response modifiers, and immunotherapy to more effectively treat patients, including tailoring such combinations to meet individual patients' needs.
- ***Prevention*** – The ultimate success in fighting cancer will be vast improvements in prevention, relying on new knowledge and tools to halt cancer from ever taking root or from progressing to a lethal form.

The 2015 challenge goal is not a prediction of what might be done; rather, it is an urgent call to do all that can be done. It will require a concerted, collaborative effort by the entire community. It will also require the simple belief—based on our ever-expanding wealth of knowledge and reliance on advanced technology—that eliminating the suffering and death due to cancer is, in fact, achievable. At the NCI, we believe that the goal is within our grasp, and we are prepared to stretch the boundaries of science, imagination, and human will to achieve success.

Andrew C. von Eschenbach, M.D.
Director,
National Cancer Institute

NATIc
National Advanced Technology Initiative for Cancer



NATIc

National Advanced Technology Initiative for Cancer

Prospectus

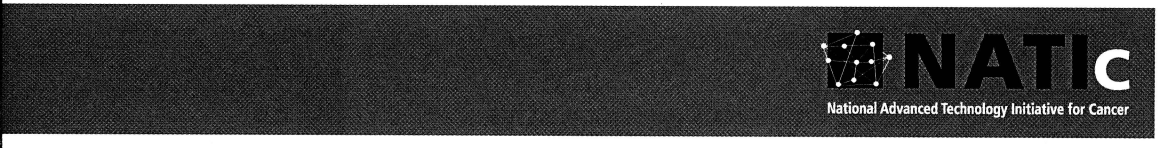
October 2004

"...for the first time in human history, we can say with certainty, the war on cancer is winnable. And this nation will not quit until our victory is complete."

President George W. Bush
September 2002

"Fighting cancer is one of our greatest priorities as a country. We cannot rest until we can prevent, treat, and cure cancer."

Secretary Tommy Thompson
July 2003



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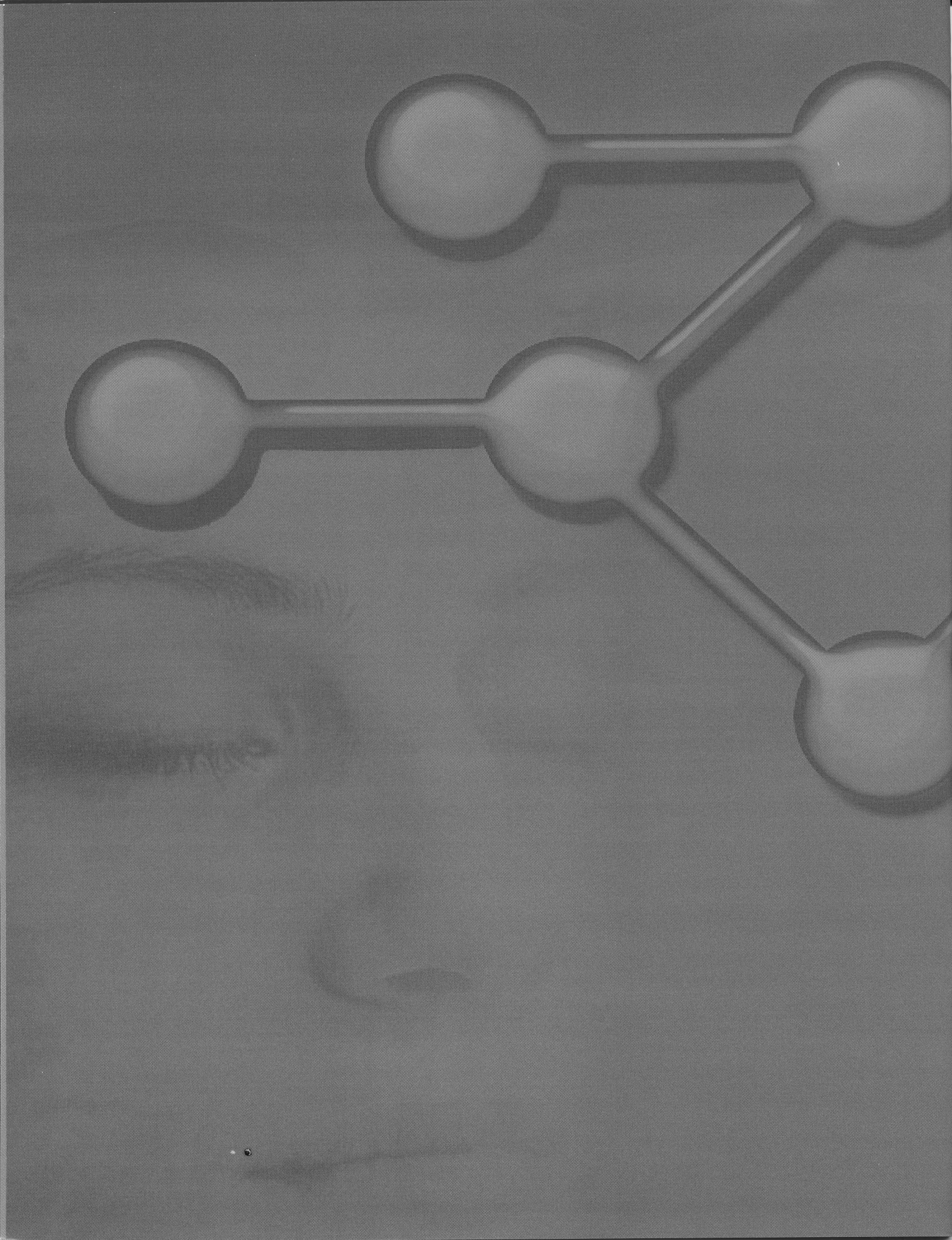
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Executive Summary

Each minute of every hour of every day, one American dies from cancer. But, there is hope. We stand at a turning point in our long struggle to conquer this disease that Americans fear most. Extraordinary advances in biomedical research that now promise exponential progress against cancer have made it possible for America to eliminate the suffering and death due to cancer. To achieve this goal and save the lives of hundreds of thousands of cancer victims, the NCI proposes to create an unprecedented national advanced technology development network—the National Advanced Technology Initiative for Cancer (NATIc). NATIc would be supported through the combination of a special congressional appropriation, NCI operating funds, and philanthropy, to deliver the revolutionary advanced technologies needed to complement the Nation's cancer research enterprise and secure the conquest of cancer.

More than 1.4 million Americans will be diagnosed with cancer in 2004, and one in two men and one in three women will receive similar sobering news in their lifetime. Although death rates for certain cancers are declining and 5-year survival for many cancers is increasing, 560,000 people will die of cancer this year and the cost of the disease will exceed $180 billion. Unless we act now, cancer will become an even greater U.S. health care burden in the next 10-20 years with the aging of the U.S. population. The NCI believes that we must act with a sense of urgency to face this challenge and has set an aggressive goal for the Nation to eliminate the suffering and death due to cancer in the next decade.

Fortunately, the United States has an extraordinary opportunity to transform cancer for its citizens and the world. By building on discoveries from basic and clinical research, we can create a new generation of advanced diagnostic and therapeutic technologies to conquer cancer and accelerate the realization of personalized medicine for every American. We now have the ability to image the functions of individual cells, to analyze proteins in a single drop of blood, and to detect changes in genes that can lead to cancer long before the disease actually develops. This is just the beginning. Through the systematic virtual integration and coordination of an unprecedented nationwide array of advanced technology development resources that will complement our cancer research enterprise, we can create the robust infrastructure required to achieve this goal.

The NATIc will consist of a national network of integrated and coordinated regional advanced technology networks (hubs) and specific specialized technology centers of excellence (nodes). The 10 hubs located across the country will consist of clusters of cancer and academic medical centers, along with State/regional R&D biotechnology centers, startup and private sector companies that are formally organized to pursue the discovery, development, and delivery of cancer interventions that will lead to elimination of suffering and death from cancer. The NCI's Federally Funded Research and Development Center (FFRDC), the Department of Health and Human Services' (DHHS) only FFRDC, will serve as a central coordinating Center and provide key core services and integration of technologies to the other hubs. Funding to establish the program over 5 years will come from three sources: an appropriation of $1.5 billion for NATIc; $500 million from NCI's operations; and $500 million from philanthropy.

This initiative will foster and coordinate advanced technology capabilities in more than 40 States and regions and align them with the Nation's cancer centers and biomedical research enterprise and national laboratories. The NATIc will accelerate the development of new breakthrough diagnostic, therapeutic, and preventive technologies for cancer, which will also have a profound impact on other diseases. More importantly, by seizing this opportunity, we can quickly close the gap between the current 5-year survival level of 65 to 100 percent—ensuring that no one suffers or dies from cancer.



Background and Rationale

One patient every minute of every day dies from cancer in America. More than half a million of our fathers, mothers, wives, husbands, loved ones, and friends will die from this disease this year alone. It is the disease Americans fear the most and they are united in their mission to conquer cancer. In addition to the human toll, cancer currently accounts for approximately $180 billion per year in U.S. health care costs. A recent study[1] estimates that reducing the cancer death rate by merely 20 percent would add an estimated $10 trillion to the U.S. economy.

In the face of these daunting statistics, due to progress in research over the past three decades (since the passage of the National Cancer Act), there is now an incredible unimagined opportunity to achieve exponential progress against cancer. An explosion of scientific knowledge of the processes leading to cancer, coupled with the rapid emergence of advanced technologies (such as genomics, bioinformatics, proteomics, and nanotechnology), has created an opportunity to achieve exponential progress against cancer. To capitalize on this turning point in the Nation's long struggle to conquer cancer, the National Cancer Institute (NCI) has established a goal to eliminate cancer as a cause of suffering and death by the year 2015.

This goal is both realistic and achievable if we take bold and aggressive action. Those threatened by cancer deserve nothing less. Recent advances in our understanding of the complex biology of cancer have provided the foundation for progress, but it will require the development and application of sophisticated technologies combined with the research enterprise to achieve our mission.

Many of the technologies needed to realize this vision are already in development: microarrays for scanning thousands of genes to find mutations in genes; combined lasers, mass spectrometers, and computers that can analyze all of the proteins in a single drop of blood; and imaging devices using light or radioactive isotopes that can "see" the chemical machinery working in a cell. Many more are in development. For example, nanotechnology devices smaller than 1/100,000th the width of a human hair can act as "biosensors" to detect genetic abnormalities, setting the stage for vast improvements in the early detection and prevention of cancer. The future of these and other research advances is dependent, in large measure, on the extent to which we can integrate our now fragmented advanced technology resources and develop a coordinated national system to ensure that advances are commercialized and delivered to patients quickly.

Although cancer is being "unraveled" rapidly at the gene, protein, and even the "nano" levels by the largest group of basic cancer researchers who have ever investigated a specific disease, we have not concomitantly created the technology development resources and seamless system needed to capitalize on their discoveries. Ironically, our understanding of the causes of cancer and many other crippling and lethal human diseases has progressed so rapidly in the past few years that the Nation's biomedical research infrastructure is not organized to foster the development and integration of advanced technologies.

The National Advanced Technology Initiative for Cancer (NATIc) is a bold new concept in biomedicine that will harness the Nation's biomedical technology resources and capabilities through a virtually integrated network of advanced technology development hubs. It will complement and capitalize on discoveries from basic research and provide the Nation with a badly needed capability to efficiently and effectively translate important scientific discoveries into the 21st century technologies that will significantly accelerate the conquest of cancer and other diseases.

[1] *Murphy, K, and R. Topel. The Value of Medical Research. University of Chicago Press, 2002*

The Proposed Initiative

The NCI proposes the creation of the National Advanced Technology Initiative for Cancer (NATIc) – a national network of new and existing resources that will identify, develop, transfer, and commercialize advanced technologies for application in cancer prevention, detection, and treatment. This initiative coupled with our academic research and health care enterprise will save hundreds of thousands of American lives, provide significant economic benefit to our States and Nation, and enable the realization of a world where cancer is a manageable, non-lethal disease.

The Nation's impressive academic research centers combined with the NCI's unique network of 61 geographically dispersed cancer centers, which are at the forefront of cutting-edge biomedical research and discovery, represent one of the key strategic elements of the proposed NATIc. Complementing this major resource are the more than 40 States and regions in the United States that have made major investments to organize

their entrepreneurial and economic development agendas around biomedical research. This combined array of advanced technology development capabilities represents an unparalleled national resource that can be coordinated and harnessed through the creation and operation of the NATIc. The NATIc will solve "breakthrough" technology problems in areas ranging from the design and fabrication of new nanotechnology-based diagnostics, to integrated functional imaging of the effects of new classes of drugs on metastatic pathways in tumors, to the development of advanced structural biology to enable the design of targeted therapies for cancer and other diseases.

The NATIc will consist of a national network of 10 coordinated regional advanced technology "hubs" and specialized technology "nodes" coordinated and managed through a combination of the NCI and leadership of the participating hubs. These advanced technology hubs will draw from regional cancer and academic medical centers, State biotechnology centers, start-up companies, venture capitalists, and private sector firms, and, in some instances, Federal laboratories to provide specific expertise and capabilities in one or more advanced technologies. Smaller nodes will be narrowly focused, generally in emerging and newer technologies. The NATIc will accelerate the application of current advanced technologies, support and optimize the development of emerging technologies, and integrate disparate technologies to create unique new therapeutic, diagnostics, and preventive cancer interventions.

The NATIc will complement and leverage the National Institutes of Health (NIH) Roadmap initiatives and capitalize on State and regional investments in advanced technology development. Although the NATIc will be cancer led, the advanced health care technologies that emanate from it will ultimately accelerate the realization of personalized medicine to improve the health of all Americans.

NATIc Operations

The NATIc will consist of 10 State/regional technology hubs. On the basis of the NCI's preliminary assessment of possible State/regional hubs, the average number of entities per hub will be approximately 5. Therefore, the program has the power to eventually link, coordinate, and synergize more than 50 entities or facilities around the Nation. To be a part of NATIc and receive funding, a hub must clearly demonstrate excellence in a specific area of advanced technology development as assessed by rigorous peer review. The hubs will be awarded competitively with funds flowing directly to all members of the winning consortia. Each of the hubs will consolidate a critical mass of specialized resources and capabilities to create an unparalleled capability in a specific technology development area. The integrated network will represent a new national advanced technology development enterprise. A key requirement for all hubs will be demonstrated ability and performance in terms of real-time coordination and integration with other hubs. Preliminary assessment of potential technology focus areas for hubs include:

- Bioinformatics and Advanced Computing
- Advanced Imaging
- High-Throughput Screening for Drug Discovery
- Proteomics, Biomarkers, and Diagnostic Platforms
- Computational and Systems Biology
- Nanotechnology
- High-Throughput Genomics Sequencing
- Biopharmaceutical Development and Scale-Up
- Biosensors and Model Systems Engineering
- Bioengineering and Advanced Prototyping

Current advances in information technologies (and bioinformatics) will allow the NATIc to operate as a virtually integrated, coordinated technology development and deployment network for the Nation. All of the NATIc's advanced technology individual hubs and nodes will interface directly with all of the others in real time. In addition, all of the participating hubs and nodes will be directly tied to the NATIc's coordinating hub, which will be located at the NCI's Federally Funded Research and Development Center (FFRDC) in Frederick, Maryland. The NATIc Coordinating Center will promote common standards and provide core resources to the member hubs and nodes and to the community at large. Strategically, the NCI-Frederick is well suited to achieving these goals through its contracting mechanisms, integrated distribution networks for data, animal models, specimens, and reagents, and platform technology capabilities. The overall management of the NATIc's virtually connected and integrated network will occur at three levels:

Senior Technical Council. This body will oversee the governance of the NATIc and include NCI's leadership, program managers, and representatives from all of the hubs comprising the network.

NCI's Program Management Group. The NCI's NATIc program managers will work with individual hubs to set up all aspects of the program, establish milestones in collaboration with the hubs and the Senior Technical Council, and monitor investments versus achievement of milestones.

NATIc Intra-hub Management and Coordination Group. A successful hub will be required to present an intra-hub coordination and management plan and organization that will oversee the functions of the hub. This plan must detail a construct for interacting with the other hubs and all aspects of program management.

In addition to their specific areas of technology development responsibilities, the hubs and nodes will compete through the NATIc's **Strategic Technology Development Program** to solve specific problems in cancer therapy, diagnosis, and prevention. The governance and management of the NATIc will determine the specific definition of these technology development programs. For this portion of the program, NATIc single and multiple-hub teams will bid to develop a specific technology platform. Final selection of one or more groups to complete the advanced technology platform will be determined on the basis of meeting specific defined milestones. All hubs and network operations and productivity will be reviewed annually.

The advanced biomedical technologies that will derive from the NATIc hold the promise of significantly impacting cancer and accelerating the realization of a personalized medicine-based 21st century health care system. In achieving these goals, the NATIc will generate significant opportunities to develop and commercialize bioscience inventions through licensing, partnerships, and new startup companies. The NCI will implement non-exclusive and cross-licensing strategies to ensure pre-competitive (public domain) intellectual property through its policies, contracts, and other agreements. These strategies will maximize the availability of pre-competitive technologies and enable the creation of integrated technology platforms by NATIc's member hubs.

Investments made through the NATIc will generate significant opportunities to develop and commercialize bioscience inventions through new startup companies. It will likely drive new public-private partnerships, as well as expand the national economy. These advanced biomedical technologies will unquestionably impact significantly across all diseases and support the creation of a personalized medicine-based 21st century health care system. At the regional level, these efforts will produce a significant economic impact on the States and areas in which the advanced technology hubs reside. The NATIc incorporates the intensity and focus of the "Manhattan Project" with the diversity and dispersion of NASA. Like these two models of American ingenuity in the face of a seemingly unattainable objective, this effort will likewise transform the future. Although these advances will be cancer focused, they will directly contribute to progress in all fields of biomedical research and biomedicine. NCI has a well-established track record in the creation and translation of advanced technologies for the benefit of other diseases in areas ranging from the identification of the AIDS virus to recent advances in the study of angiogenesis to developing new treatments for several major diseases.

Financial Summary

Figure 1 illustrates the overall organization of the NATIc in terms of sources of funds, NCI program development and management, and the outlay of resources to the 10 advanced technology hubs and a selected number of specialized technology nodes. The figure also illustrates the dynamic nature of the NATIc, which will operate as a virtual, interactive, collaborative network where ideas, information, and technologies will flow throughout the overall system in real time.

Table 1 summarizes the funding sources, resource totals, and the obligation and outlay plans for the NATIc. The NATIc will be developed using an innovative combination of funds from the Federal Government and private and institutional philanthropy. Sixty percent, or $1.5 billion, will be available as NATIc appropriations over 5 years.

The NCI pledges to raise $0.5 billion in philanthropic funds to support the NATIc through the Foundation for the National Institutes of Health, Inc. Finally, the NCI will also redeploy $0.1 billion each year for 5 years to support the NATIc from its annual Federal appropriation, and will continue to support the NATIc at a level of approximately $0.1 billion per year when the NATIc appropriations end in FY 2010.

The major organizational unit of the NATIc will be the State/regional technology hubs. Each hub will represent a consortium of four to six organizations and institutions. The NATIc will fund approximately 10 State/regional technology hubs. These 10 hubs will include up to 50 participating entities from States and regions across the United States. These advanced technology hubs may be led by NCI's Cancer Centers, academic medical centers, engineering schools, State and regional

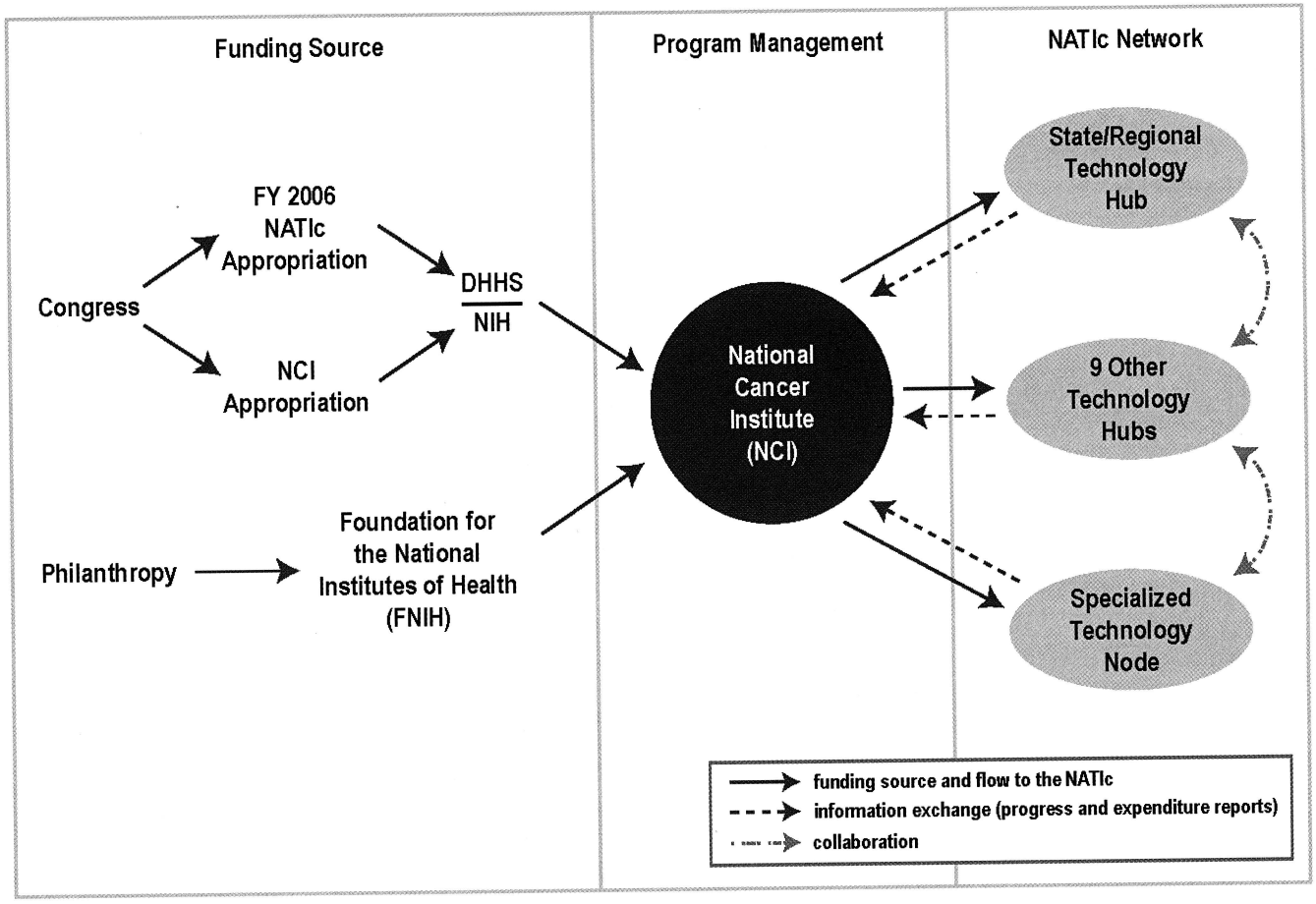


Figure 1. NATIc Organization and Funding Streams

Table 1. Summary of Funding Sources, Obligations, and Outlays for the National Advanced Technology Initiative for Cancer (dollars in millions)

FUNDING SOURCES	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
NATIc Appropriation	$300	$300	$300	$300	$300	$1,500
NCI Appropriation	100	100	100	100	100	500
Philanthropy	100	100	100	100	100	500
Total Funds	**500**	**500**	**500**	**500**	**500**	**2,500**

OBLIGATIONS	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
State/Regional Advanced Technology Hubs 1/	$205	$268	$269	$269	$269	$1,280
Specialized Technology Nodes 2/		10	10	10	10	40
Strategic Technology Development Program 3/	266	191	190	191	191	1,029
National Coordinating Center at NCI-Frederick	20	20	20	20	20	100
Management and Support 4/	9	11	11	10	10	51
Total Obligations	**500**	**500**	**500**	**500**	**500**	**2,500**

OUTLAYS	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011-FY 2014	Total
State/Regional Advanced Technology Hubs	$83	$159	$215	$251	$266	$306	$1,280
Specialized Technology Nodes		4	7	9	10	10	40
Strategic Technology Development Program	106	144	177	192	196	214	1,029
National Coordinating Center at NCI-Frederick	9	14	17	19	20	21	100
Management and Support	8	11	11	10	10	1	51
Total Outlays	**206**	**332**	**427**	**481**	**502**	**552**	**2,500**
Portion from Federal Funds	**{166}**	**{267}**	**{342}**	**{385}**	**{402}**	**{438}**	**{2000}**

1/ Total number of entities funded: 50 within 10 State/regional advanced technology hubs.

2/ Total number of entities funded: 10 within 5 specialized technology nodes.

3/ The authority to make awards utilizing the "Other Transaction" authority should be included within the NATIc Appropriation.

4/ An increase of 30 FTEs to the current FTE ceiling would be required to perform inherently governmental functions.

centers of biotechnology and innovation, or other qualifying nonprofit organizations. Ninety-four percent of the funding for the NATIc will ultimately be obligated and distributed to the organizations comprising the hubs and nodes. Obligations of funds will be directed through four distinct categories of awards: the advanced technology hubs (State/regional technology hubs); specialized technology nodes; and the National NATIc Coordinating Center, located at the DHHS Federally Funded Research and Development Facility (FFRDC) at Frederick, Maryland. Once qualified through peer review and funded, the hubs will be eligible to bid on specific Strategic Technology Development Programs.

Each of the projects funded through the Strategic Technology Development Program will be defined in terms of the advanced technology deliverable required, and each successful bidder will be required to meet milestones and deliver a product or prototype technology at the conclusion of a specific program. Design and management of the advanced technology hubs and specialized technology nodes, monitoring of milestones, and priority setting will occur through a combination of NCI program staff and the NATIc's Senior Technical Council.

The mechanisms proposed to establish the hubs and implement the Strategic Technology Development Program of the NATIc represent a new model specifically designed to optimize and accelerate the creation of innovative, targeted therapeutics, diagnostics, and preventive cancer technologies. This model places significant emphasis on creating the NATIc's network of advanced technology hubs as effectively and rapidly as possible. It is anticipated that the increased flow of intellectual property from the NATIc will provide a major impetus for the State/regional centers of innovation and biotechnology to increase their level of investment in technology transfer and company formation. This bioeconomic model promises to provide an opportunity for the NCI to "sunset" its ongoing funding

for the NATIc after 2014; however, if needed, the NCI would continue to invest at a level of $100 million per year to maximize the flow of advanced cancer technologies to patients.

Benefits and Returns to the Nation

The biggest returns from the NATIc in the next decade will be measured in human terms. Eliminating suffering and death due to cancer (at current mortality rates) will save more than 560,000 lives per year in the United States alone and eliminate one of the biggest public health problems that America faces in the next two decades. Of greater importance, countless numbers of years of high-quality life will be restored to patients. Assuming current cancer incidence rates, the NATIc could result in a significant increase in numbers of 5-year survivors on an annual basis, culminating in 100 percent survival in 10 years.

The progress needed to realize these returns will be achieved by the integration with our Nation's cancer and biomedical enterprise that will comprise the NATIc. Due to the breadth and depth of the NATIc's virtual advanced technology development capacity, targeted cancer drugs and devices that today are years away can be achieved in months to a few years. The availability of nearly any expertise and advanced technology platform, along with scale-up and prototyping capabilities of the NATIc, will foster exponential progress against cancer and other diseases. The foundation for this progress will be tied to the development of NATIc's strategic national biomedical platform technologies such as a common bioinformatics grid, and to the integration of physics and microchip technologies with engineering and medicine.

The flow of technical milestones and deliverables over the life of the NATIc will begin with the integration of the hubs through the NCI's Cancer Bioinformatics Grid (caBIG) and proceed through the development and adoption of key common technology platforms such as a national biospecimen resource. Technical milestones will be met, and advanced biomedical technologies to detect, treat, and prevent cancer produced through the virtually integrated advanced technology network of hubs. The hubs will work with the NCI's Strategic Technology Development Program to develop these specific cancer technologies. Key lifesaving advances will accrue from the NATIc throughout the planned period of funding and well beyond. Overall, some of the expected contributions to the research enterprise currently supported by NIH and NCI include the following:

- National biospecimen resource to support all post-genomic research
- Cancer bioinformatics network that connects all scientists, clinicians, and components of the cancer research and health delivery enterprise
- Catalogue of every genetic abnormality that serves as a basis for all types of cancer
- Comprehensive set of protein biomarkers that identify every type of cancer
- Functional molecular imaging platforms to diagnose cancer, guide therapeutic delivery, and monitor treatment response
- Fifty new targeted drugs for cancer treatment and/or preventives in clinical trials with 20-25 entering the marketplace
- Diagnostic nanotechnology and other platforms to identify all significant abnormal proteins in a drop of blood
- A seamless system of drug development, including clinical trials that require 5 years or less from lead compound identification to regulatory approval
- "Smartcard" supported clinical trials system to create transparent, patient-friendly trials connected to electronic-medical records
- Systems biology understanding of all the abnormal pathways in cancer cells to support cancer prevention, early detection, and treatment

Finally, the economic returns from the NATIc will be substantial. It will most certainly have a significant impact on the overall cost of cancer in the United States, a major portion of which comes from years of life lost due to premature death from cancer. A major portion of the over $180 billion annual economic burden of cancer derives from the value assigned to years of life lost due to premature death from cancer. The advanced health care technologies from the NATIc offer an unprecedented opportunity to increase disease-free survival that will significantly reduce the overall cost of cancer. For example, advanced functional imaging technologies will enable early diagnosis and treatment of diseases such as breast cancer. More than 48,000 women lose their lives each year to breast

cancer. Advanced diagnostics and therapeutics could quickly reduce breast cancer mortality by as much as 20 percent, which would mean saving an additional 10,000 lives and reducing health care costs by $1.4 billion annually.

In addition, the NATIc will significantly increase opportunities for commercialization of advanced health care technologies. The NATIc hubs could provide unprecedented economic impetus in selected States and regions with significant strengths in an alignment of advanced technologies. The economic development effects in terms of new high-technology job creation could be significant in States and regions that have invested to support advanced biomedical "clusters" such as California, Florida, Georgia, Maryland, Massachusetts, Michigan, North Carolina, Ohio, Pennsylvania, Wisconsin, and several others.

Summary

The NATIc is a revolutionary concept to harness the highly sophisticated array of resources that have evolved from our Nation's commitment to biomedical research, the NIH Roadmap initiatives, and the State/regional capabilities in advanced technology development for biomedicine. Funded at $2.5 billion through a Federal, philanthropic, and private partnership, it will create an unprecedented virtual network of advanced technology hubs that will coordinate and leverage the resources of cancer and academic centers, State and regional centers of biotechnology and innovation, national laboratories, and other partners. This virtually connected network provides a revolutionary approach to developing the advanced biomedical technologies needed to achieve the NCI's goal of eliminating suffering and death due to cancer in a decade.




DEPARTMENT OF HEALTH & HUMAN SERVICES · USA
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MEETING REPORT

Leveraging Multi-Sector Technology Development Resources and Capabilities to Accelerate Progress Against Cancer

A National Cancer Institute Roundtable

FAIRMONT HOTEL
WASHINGTON, DC
JANUARY 20-21, 2004

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





Executive Summary

On January 20-21, 2004, the National Cancer Institute (NCI) convened a pioneering leadership roundtable in Washington, DC, of visionaries representing our Nation's cancer centers; biotechnology, pharmaceutical, imaging, information, diagnostics, and other companies; financial markets and investment banking communities; Federal, State, and local health agencies and government offices; and philanthropic organizations and cancer survivor/advocates. The forum, entitled "Leveraging Multi-Sector Technology Development Resources and Capabilities to Accelerate Progress Against Cancer," examined the scientific, societal, cultural, and economic barriers to meeting this goal and offered multi-sector solutions that will enable its achievement and ultimately impact the Nation's cancer burden.

This unprecedented forum explored State, regional, philanthropic, and other model programs of strategic technology resource integration that optimize and accelerate the discovery, translation, development, and commercialization of advanced biomedical technologies. Mechanisms that ranged from providing investigators access to technology incubator facilities to investment support for entrepreneurial activities, set these models apart and drive new bioeconomic development initiatives. The discussants envisioned the creation of a collaborative "fabric" from existing models that would more effectively leverage assets through the alignment of resources and expansion of partnership opportunities to achieve the NCI's goal "to eliminate suffering and death due to cancer by 2015." The Roundtable members were asked to address the following challenges:

- Identify key barriers that stand in the way of optimizing the timely transfer, development, and commercialization of advanced biomedical technologies (including incremental and disruptive technologies) to accelerate progress against cancer.
- Explore key regional, national, and other models whereby advanced biomedical technologies are successfully identified, transferred, and ultimately commercialized for broad patient benefit.
- Brainstorm and evaluate novel concepts to facilitate the strategic alignment of resources and capabilities from all sectors to remove mission-critical barriers and design novel, innovative approaches to speed the development and delivery of new diagnostics, preventives, and treatments for cancer.
- Suggest actions that can be undertaken by the appropriate sectors.

A series of expert panels described the technology development pathway and identified key barriers to development, including venture financing gaps; multidisciplinary collaboration (team science); regulatory requirements; intellectual property rights; risk-sharing; data-sharing; and platform technologies. The panels highlighted innovative State, regional, Federal, and not-for-profit models of

technology transfer and development that surmount many of these barriers. Building on these presentations, the Roundtable leaders framed critical barriers and brainstormed solutions to overcome them.

Roundtable participants prioritized the obstacles (scientific, policy, organizational, and economic) to developing key cancer technologies into four critical challenge areas:

- The need for **cross-disciplinary collaborations**
- The widening **"gap" between late discovery and early development** of diagnostics and therapeutics
- The critical **lack** of available **standards** (for data description, collection, reporting, etc.)
- The requirement for **cross-cutting technology platforms**

Four Approaches to Eliminating Major Barriers

The Roundtable discussions produced a wide array of recommended actions to counteract the barriers identified and in several cases offered metrics to assess progress in overcoming them. Taken together, these actions could inform new visions for optimizing and accelerating the development of advanced biomedical technologies for all of the sectors represented at the Roundtable—as individual entities and in new alliances and partnerships.

Building Cross-Disciplinary Collaborations and Teams. Future breakthroughs in cancer will require an integration of knowledge about the fundamental processes and interactions that define cancer. Major achievements in innovative technology will derive from a systems biology approach to understanding cancer. Systems biology will enable the development of advanced technologies that will improve both efficiency of resources applied and utility of products. The Roundtable suggested that two to three collaborative technology teams be assembled using a hub (leadership) and node (specific expertise) model that are accountable in terms of deliverables and team performance. The teams should be supported at an appropriate level for five years and include funds for training across disciplines, with an emphasis on clinical development and optimal interaction among team members. Teams should be region based to improve interteam interactions and built with sustainability beyond the five-year period of NCI support. Furthermore, the Roundtable recommended that funding mechanisms take advantage of innovative Federal models (such as In-Q-Tel or Homeland Security Advanced Research Projects Agency) that focus on specific outcomes and use a project management mechanism to reach defined milestones.

Bridging the Gap Between Late Discovery and Early Development of Diagnostics and Therapeutics. To reduce the failure rate of post-genomic diagnostics and therapeutics entering clinical trials, with the associated waste of

financial and intellectual resources, the Roundtable proposed that a series of interrelated goals and metrics be established as follows:

- Enroll 100,000–1,000,000 patients in clinical trials that are captured and the patient biospecimens and clinical outcome data made widely available.
- Develop 100 new mechanism-based investigational new drug (IND) applications, at least 50 of which involve multiple combination therapies (more than one moiety provided in a delivery system).
- Develop a "best-practices" standard for IND submission and conduct of clinical trials and establish a system for certifying the quality of clinical trial design.
- Design and deploy financial models for late discovery/early development activity, (including new cancer technologies) led by public/private partnerships that could be initiated by the venture capital groups and philanthropic organizations.
- Redirect the Small Business Innovation Research (SBIR) program to concentrate on targeting late discovery/early development research, and to allow organizations with venture capital support to participate in the program.

To reach these goals, the Roundtable suggested that the NCI enable a project management structure with responsibility to identify likely partners, create timelines for development, and establish quality standards. An advisory board drawn from academia and industry should also be formed that could review technology development plans and aid in the prioritization of new ideas for development, In addition, legislative action should be encouraged (1) to increase time for patent exclusivity for oncology products similar to that for pediatric exclusivity, and (2) to grant the NCI authority to use existing innovative models for funding and directing late discovery/early development activity (e.g., Defense Advanced Research Projects Agency models). It was also suggested that a mechanism for financial risk-sharing among the venture community, private foundations, and a structure like the Foundation for the National Institutes of Health (FNIH) should be developed with cancer as a focus. Finally, the Roundtable participants noted the NCI's Frederick facility, could develop an appropriate screen (e.g., component of the National Advanced Biomedical Technology Initiative) designed to improve the pharmaceutical properties of drug candidates. This would substantially lower the risk of drug development and increase the interest of the pharmaceutical companies in developing new cancer drugs.

Developing Data Standards. Improving the efficiency with which cancer researchers can access and utilize data generated from both basic research and clinical trials would have a profound effect on the rate of technology transfer and development of novel therapeutics and diagnostics for cancer. Today, this very obvious developmental need is hampered by a lack of data standards that prevents data-pooling and comparison. To achieve the goals of (1) creating standards for identifying and validating biomarkers, (2) reporting clinical data that can be used in both research and clinical arenas, and (3) reporting molecular and structural data with a goal of increasing access to and utilization of shared data, the Roundtable proposed that the NCI and industry partners convene a consensus meeting for

defining the structure of such standards. Ownership of the standards should be defined through an organization that would assume responsibility for managing the standards. The standards development effort should become a global effort as soon as feasible, perhaps through an alliance with the Organisation of Economic Co-operation and Development based in Europe. The NCI must drive change in the clinical and research communities to accept open source access to data, perhaps by linking funding access to standards compliance. Finally, an NCI-led task force should be convened and authorized to review and publish standards—and provide a "seal of approval" for the field.

Developing Cross-Cutting Technology Platforms. Accelerating the development of novel therapeutics and diagnostics for cancer will require the identification and creation of cross-cutting technology platforms in areas such as bioinformatics, proteomics, and nanotechnology. To meet these goals, the Roundtable encouraged the NCI to take a leadership role by establishing development demonstration projects (with a defined technology focus) in selected emerging fields. One such project should be identified and operational within six months. The NCI should also lead an effort to create and disseminate initial standardized data sets for platforms that can serve as foundations for adding data to larger databanks, along with simple data collection tools to capture existing data in these databanks. To effectively implement the development of these platforms will require an immediate inventory of the biomarkers and platform technologies available today. An advisory panel of researchers from academia and industry, convened by the NCI, could identify the technologies that are needed to enable an emerging area such as systems biology research. Federal funding should be provided for the development of a system for real-time monitoring of datasets. This could be based on systems that other technology-based agencies, such as the U.S. Department of Defense (DoD), the National Aeronautics and Space Administration (NASA), and the U.S. Department of Homeland Security's (DHS) Homeland Security Advanced Research Projects Agency (HSARPA), have already developed for this purpose. Finally, to achieve its 2015 goals will require that the NCI lead the development and dissemination of standardized platform hardware and software and work with public and private sector organizations to establish a data framework that will capture data from all specialized technology platforms.

Summary and Next Steps

The Roundtable emphasized that neither the NCI nor any other single sector can break through these barriers. Only the combined and coordinated efforts of all parties in the Nation's cancer research and development enterprise, including other Federal agencies such as the U.S. Food and Drug Administration (FDA) can ultimately succeed. Participants noted that the NCI can lead much of this effort by spearheading the transformational work needed, both inside and outside the NCI, to more efficiently turn great science into great clinical advances for the diagnosis and treatment of cancer. In particular, the Roundtable noted that newly established

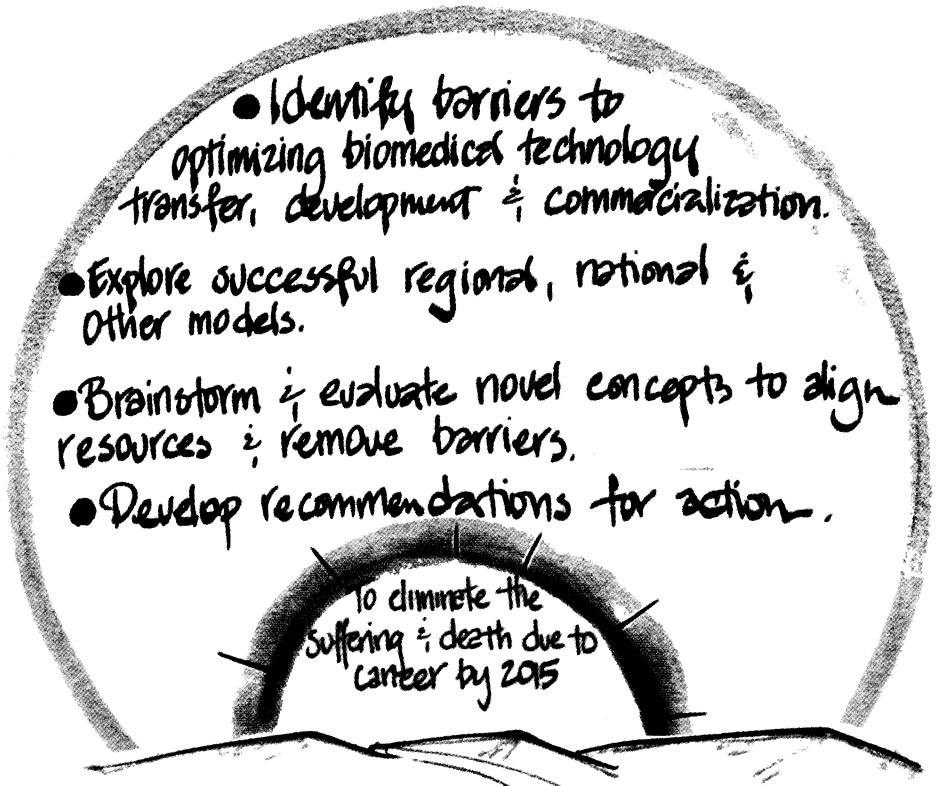
partnership between the NCI and the FDA bodes well for increasing the rate and number of new diagnostics and therapeutics that will reach cancer patients.

In describing the future, the Nation's cancer centers were viewed as a key resource base and central area of focus for the development of advanced cancer technologies. These centers will act as "hubs" for investment and partnerships, leverage State and regional development capabilities, and drive economic development. Such regional efforts can drive the entrepreneurial development needed to convert promising technologies into highly effective diagnostics and therapeutics for cancer.

The roundtable participants cited a need for new funding mechanisms. It was recommended that new resources streams, derived from all sectors, be developed to specifically support the need for advanced cancer technologies. Furthermore, participants felt that the development of these resources streams should occur in a manner that preserves and strengthens the Nation's basic/discovery research "engine" that drives development. Participants looked to the leadership of the venture capital investment sector to inform approaches for capital and risk-sharing collaborations. These focused on a variety of funding sources, including the increasing number of nonprofit, health-related foundations with cancer-related missions. It was further suggested that a forum be convened that would bring the financial and philanthropic sectors together to work on financing and project management strategies that would enable the development of advanced cancer technologies. This alliance could be a critical step in providing momentum to accelerate the pace of targeted therapies, preventives, and diagnostics for cancer. In turn, such collaborative financing models could serve as models for biomedical research and development.

This unprecedented Roundtable reinforced that the future depends on building new partnerships across the cancer enterprise. The meeting produced a large number of suggestions for actions that can be taken by the NCI and other sectors to remove the major barriers that slow or block the development of the advanced cancer technologies needed to accelerate progress against cancer and meet the 2015 challenge. The range of ideas for actions is reflected in the appendices, and several key near term actions from each of the four key focus areas are highlighted in the body of the report. In fact, several of the actions are already underway, either led by the NCI or other Roundtable participants. For example, unique funding and technology development models are being actively evaluated for their applications to cancer and specific ideas for "credentialing" cancer targets are being explored to address the late discovery to early development gap. Overall, the Roundtable produced a wealth of substantive solutions that can be pursued singly or through collaborations, consortia and alliances.

LEVERAGING MULTI-SECTOR TECHNOLOGY DEVELOPMENT RESOURCES & CAPABILITIES TO ACCELERATE PROGRESS AGAINST CANCER



TUESDAY Discovering Barriers

- Opening
- The Role of Advanced Bio-Medical Technologies in the Conquest of Cancer
- PANEL 1: The Cadorted Continuum of Discovering & Developing adv. Bio-Med. Tech.
- BRAINSTORMING SESSION
  - KEYNOTE ADDRESS: Accelerating Medical Solutions
- PANEL 2: Models of Regional-State Panel
- PANEL 3: Innovative Non-Profit Models
- Prioritizing the Barriers

WEDNESDAY Developing Solutions

- Opening & Review
- The Future Isn't What It Used to Be
- PANEL 4: An "Outside-the-box" Federal Model
- GROUP SESSIONS: Barriers & Solutions
  - KEYNOTE ADDRESS: HSARPA's role in developing advanced technologies for homeland security
- PANEL 5: Putting the Models To Work
- PANEL 6: Can Cancer Centers Serve As Major Vehicles?
- Prioritization
- Actions & Next Steps

Meeting Report*

DAY 1

Identify the barriers to accelerating the development of advanced biomedical technologies to conquer cancer by 2015

The academic, business, investment, philanthropic, and government leaders who participated in the National Cancer Institute (NCI) Roundtable "Leveraging Multi-Sector Technology Development Resources and Capabilities to Accelerate Progress Against Cancer" were presented with the magnitude of the current and future cancer epidemic and the Institute's challenge goal—to eliminate the suffering and death due to cancer by 2015. This will not be an easy road, as there are significant barriers to developing and delivering the advanced technologies that will be required to achieve this challenge.

Demographers and economists predict that cancer will become a major health care crisis in as few as 10 years. In the United States alone, it is estimated that one person in the United States dies each minute from cancer, and 560,000 lives will be lost this year. And this is the tip of the iceberg—the confluence of the aging of the baby boomer generation, demographic shifts, and the predominance of cancer in individuals age 50 and over portend significant increases in the numbers of cancer cases and staggering economic costs. The cost of cancer was approximately $180 billion in 2003 and could grow to trillions of dollars annually unless we act now—which calls for a comprehensive strategy and plan of action.

This Roundtable was convened for leaders from all of the sectors that make up the cancer enterprise to share their knowledge, vision, and commitment to inform new strategies that could drive and streamline the advanced technology development needed to achieve the NCI's 2015 goal.

Dr. Andrew von Eschenbach—Opening Challenge

In welcoming the Roundtable participants, Dr. Andrew von Eschenbach, the NCI Director, underscored the importance of leveraging resources through new partnerships as a cornerstone of reaching the NCI challenge goal to eliminate the suffering and death due to cancer by 2015. In reflecting on the modern era of cancer research, he noted that the crusade began on December 23, 1971, with the signing of the National Cancer Act. This propelled the Nation on a new trajectory for research and scientific pursuit that has resulted in many innovations and breakthroughs in our collective understanding of cancer biology. He reflected on the obligation and tremendous capacity of the NCI to be an integrating force and change agent among the constituent stakeholder communities engaged in the fight against cancer.

* Facilitation by Robert Mittman and graphics by Tom Benthin

Due to unimagined advances from the investments that the NCI, the NIH, and others have made in biomedical research, it is now possible to envision a world where patients will live high-quality lives and not die from cancer. The NCI's leadership role in catalyzing and supporting the continuum of cancer research, creating an unparalleled cadre of basic and clinical investigators, optimizing the development of excellent health care institutions, and engaging cancer survivors as partners has set the stage for unparalleled advances against cancer. After more than three decades, the cancer research community is poised at a strategic inflection point. Progress from this inflection point forward could be exponential, but only if we are able to capitalize on the powerful fruits of discovery/basic research. Accelerating the trajectory of progress will depend in large measure on our ability to develop and integrate the advanced technologies needed to diagnose cancer early, prevent it, and treat it with targeted agents.

Our understanding of cancer as a process, coupled with the power of advanced technologies to intervene in this process, provided the basis for the challenge goal to eliminate the suffering and death due to cancer by 2015. To achieve the goal will require a new strategy that integrates the continuum of discovery, development, and delivery and new paradigms for optimizing and accelerating this process. Accelerating "throughput" across this continuum requires new financial resources, enabling technologies, and unprecedented intellectual capital that interfaces with the impressive array of infrastructure and knowledge resources that already exists in the cancer R&D enterprise.

The NCI has undertaken a number of strategic initiatives to provide key infrastructure, partnerships, and new paradigms for advanced technology development. For example, the NCI is developing a plan for a National Advanced Biomedical Technology Initiative (NABTI) for cancer. This initiative would create a nationwide capability in advanced biomedical technology development that could provide the impetus for progress in cancer and concomitantly strengthen the biotechnology industry, which is so important in achieving the 2015 goal.

To capture the vision of what is possible, Dr. von Eschenbach reflected on how a dream can become reality. In 1976 a young man diagnosed with metastatic testicular cancer would have no hope to be alive today. Yet today, Lance Armstrong is not only a cancer survivor but also a five-time winner of the Tour de France. Dr. von Eschenbach concluded that this dream could become reality for many, but it will depend on the participants in this Roundtable and leaders all across the cancer community coming together to build a new "ecosystem" that integrates knowledge, technology, resources, commitment and will. The 2015 challenge goal is achievable, and we should settle for no less.

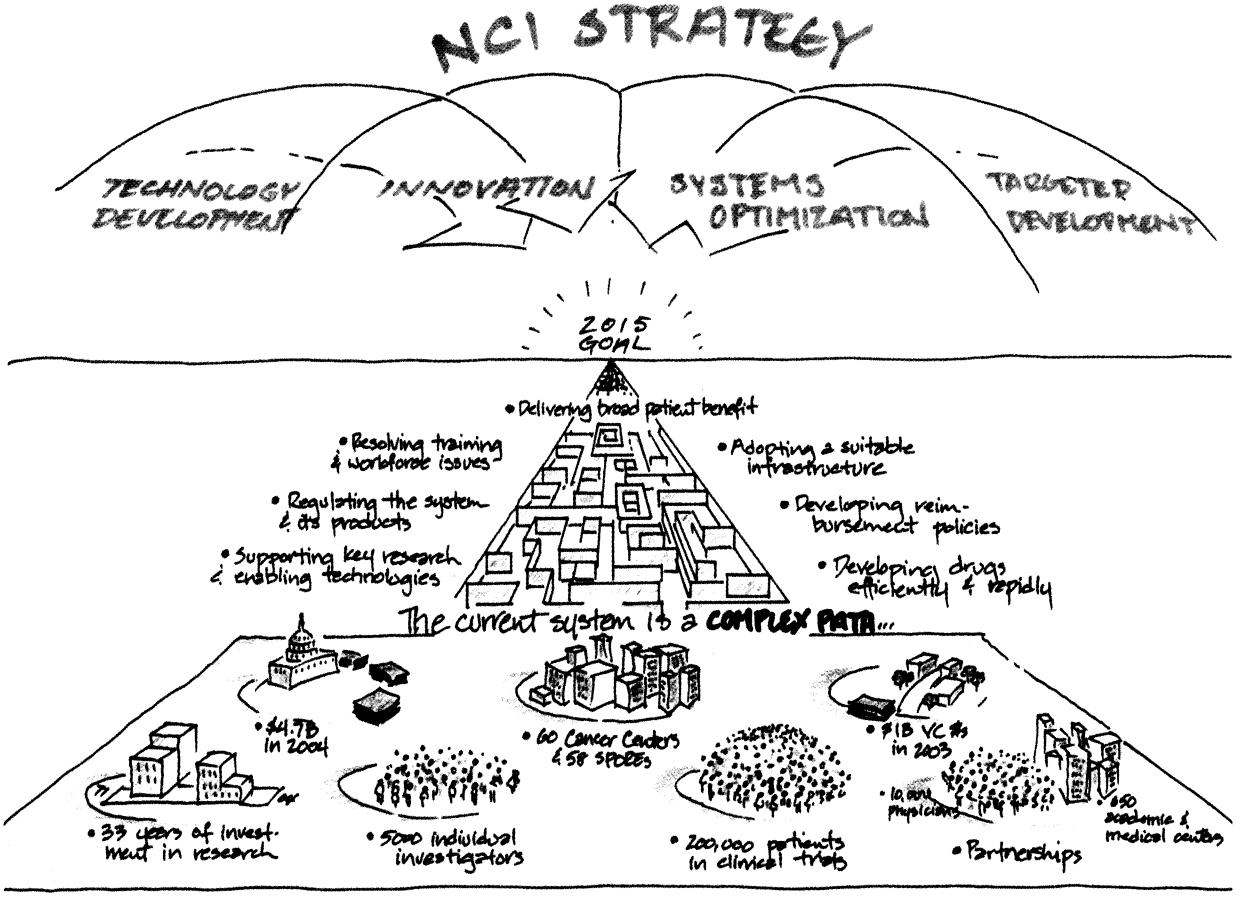
Dr. Anna D. Barker—The Starting Point: Existing Resources and Future Challenges for Advanced Technology Development in Cancer

Dr. Barker, NCI Deputy Director for Advanced Technologies and Strategic Partnerships, gave an overview of the NCI's vision for future advanced technologies for cancer and set the stage for the two days of focused attention on developing multi-sector strategies to optimize the development process. A substantial national cancer research and development resource base exists that can be leveraged to accelerate the development and integration of advanced technologies for cancer. The largest infrastructure ever assembled to attack disease has been built during the past 33 years of investment in basic research. The NCI's budget for fiscal year 2004 of $4.7 billion represents the largest annual investment dedicated to the conquest of cancer to date. These resources support the laboratory and clinical research of more than 5,000 highly skilled investigators who are primarily located in the NCI's 60 designated cancer centers and 58 Specialized Programs of Research Excellence (SPOREs). Many of these major research platforms work in active partnerships with over 650 academic health centers and 10,000 physicians to provide a nationwide network of basic and clinical cancer research and care. The more than 200,000 cancer patients who participate in NCI-sponsored clinical trials also enrich the research base. Furthermore, it is estimated that nearly $1 billion in venture capital investments in cancer research were made in 2003, which is critical for technology development.

Even in the face of this major national infrastructure and significant capabilities base dedicated to cancer research, the current system of drug and technology discovery, development, and delivery is a complex and often unsuccessful endeavor. This "system" is encumbered by a complex of issues and barriers including (1) high costs and inefficiency of the drug development process; (2) need for sustained investment in high-impact and enabling technologies; (3) required regulatory processes for market entry; (4) complexities of establishing reimbursement structures for cancer diagnostics and therapies; (5) training of the health care workforce for technology delivery; and (6) establishment of a health technologies delivery system to ensure maximum patient benefit for all those in need.

The NCI recognizes that the cancer drug development pipeline contains serious rate-limiting steps and is actively working to overcome them. For example, one critical component is the regulatory process, and the NCI has partnered with the FDA to create a joint task force to develop a common interface for discovery and regulatory science. As another example, the NCI is launching a major bioinformatics platform, the Cancer Biomedical Informatics Grid (caBIG), to provide connectivity, develop common solutions to problems (e.g. clinical trials reporting), and promote standardization of informatics tools across the cancer community. The NCI is also taking an active role in developing a distributed national resource of biospecimens that are annotated with clinical and genomic data to facilitate critical research such as biomarker discovery and validation.

INTEGRATION OF THE TECHNOLOGY DEVELOPMENT PARADIGM



As introduced by Dr. von Eschenbach, the NCI is also engaged in planning for a National Advanced Biomedical Technologies Initiative (NABTI) to facilitate the development and integration of advanced cancer technologies. This national technology initiative will include a series of connected technology "hubs" and "nodes." The NCI-Frederick campus is proposed as a major "hub" for this initiative; to provide support for advanced technology development in key areas ranging from bioinformatics to advanced imaging and prototyping. Planning for this initiative currently involves both the intramural and extramural scientific communities. It is anticipated that the NABTI will provide State and regional centers of innovation and technology development new impetus for the development of advanced technologies for cancer. It should be noted that many of these successful regional technology clusters are closely allied with the NCI's major cancer centers. In

improving the pace of technology development for cancer, the NABTI could also provide support for a high-technology-based bioeconomic development model. Finally, the success of the NABTI will significantly depend on effective partnerships, especially with progressive companies and investors interested in accelerating the conquest of cancer as part of their commercial strategy.

Panel 1

The "Contorted" Continuum of Discovering and Developing Advanced Biomedical Technologies

Discovery and basic research have yielded an incredible knowledge base and fundamental understanding of the body's mechanisms and processes at an ever-increasing level of specificity. In the past few years, especially since the sequencing of the human genome, the complexity of cancer is being increasingly "unraveled" at the gene, protein and even nanolevel (molecules and atoms). If we can more effectively enable discovery and optimize and accelerate development, it will be possible to capitalize on the inflection point that now exists and deliver highly effective interventions to cancer patients. Lessons from the business and R&D enterprises have the potential to bridge the gaps in the continuum of discovery and development and set a new course for realizing breakthrough cancer technologies.

There are three sequential stages of technology development as described by **Mr. Stephen Fodor,** CEO of **Affymetrix.** The first, assessing the feasibility of technology and its application, is truly high risk and is dominated by Federal R&D funding. The second and third stages reflect development and industrialization processes that are generally supported by venture capital markets and private investors, respectively. Integration of these stages is the key to success. Success can only be achieved through high-level planning with a clear vision, providing firm objectives for each sector, defining distinguishing features between basic and goal-oriented research, setting goals and endpoints, and tying accountability to performance. Public-private partnerships are key to successful strategies, particularly in biotechnology, as they reduce development costs and duplication of infrastructure and services.

Basic discovery research has established an unprecedented new opportunity for the technology marketplace in cancer detection that is largely underpinned by our knowledge of the genetic and molecular basis of cancer. A well-reasoned strategy for early detection is a major requirement for achieving the 2015 goal. **Dr. Lee Hartwell,** President of the **Fred Hutchinson Cancer Research Center,** described a vision for an emerging era of molecular diagnostics that will have a dramatic impact on the clinical management of cancer. The processes of staging of cancer, assessing patient response to therapy, and integrating new platforms for diagnosis and treatment delivery could soon revolutionize approaches to cancer. However, virtually none of the technology and infrastructure needed to realize the health payoffs from the Human Genome Project and basic cancer research exists in today's medical systems. How do we go about making this a reality? One suggestion is a "hub and spoke"

model of interconnected technology centers. The core systems of reagents, platforms, standards, and model systems must be developed now to accelerate the process of building these capabilities. Another vital step is the redefinition of the interfaces between the academic and commercial sectors. Strategic partnerships by academic research institutions, beyond the traditional pharmaceutical and biotechnology sectors, into areas of computation and engineering sciences will be crucial to achieve this goal. One important area is the application of proteomics technologies to the problem of identifying large number of tumor markers (biomarkers) from body fluids rather then directly from a tumor. Although the science of proteomics is receiving a lot of attention, there is currently no technology that is up to the task of handling the diversity and dynamic range of these proteins needed for early detection. That then, according to Dr. Hartwell, is where a technology development effort should occur, and while the cancer field recognizes this critical need, there is currently a need for direction and alignment to accelerate progress.

Dr. David Parkinson, Vice President of Oncology for **Amgen,** spoke to the need for a new system to optimize cancer therapeutic development and provided some examples in support of his rationale. He noted that tumors are still classified—and the type and course of therapy determined—using antiquated pathological classification systems. This continues despite clear evidence that the biochemical and genetic characteristics of tumors, not their physical appearance, determine whether a given therapy will be successful. He noted that the problems confronting cancer therapeutics development are clear, but the development of the advanced technologies required to take advantage of these scientific discoveries are lacking. He proposed that some of the most important features of the current drug development system that must be aligned include the creation of more efficient clinical trials infrastructure, robust bioinformatics, better technologies to biologically describe cancer in patients; and a clear regulatory approval pathway built around the science of biomarkers instead of remote clinical endpoints.

Moving from the research, development, and commercialization continuum, **Mr. David Morgenthaler,** Founding Partner of **Morgenthaler Ventures,** moved the conversation to examine how the development of advanced cancer technologies can be financed. The practicalities of today's technology commercialization pathway reflect some startling concerns for cancer. He called attention to the mismatch between capital requirements and development time on the one hand, and the return on capital expected by those investing in technology development on the other. Although biotechnology investment has relied largely on traditional venture capital avenues, it is clear that advances in science have created a situation where some of the most promising technologies cannot secure the necessary financial backing at critical junctures. This is worsened by what has to date been a meager return on investment realized by biotechnology investors, even when compared with the return on U.S. treasury bonds. Innovative risk-sharing models that utilize goal-oriented, product-focused development plans are needed to bridge the gap in funding. Inherent in this problem of bridging the late discovery-early development gap is a need to better define and protect the intellectual property that drives both

technology development and eventual return on investment. There are signs of improvement on the horizon, which is reflected in the substantial capital available for developing cancer diagnostics and therapeutics. However, this capital is generally available only when the technologies reach the later stages of clinical development. The lesson of the past is that developing advanced cancer technologies will require that we address this funding gap through innovative partnerships and collaboration. He stated that a national strategy to achieve the 2015 goal requires that the NCI define problems that are ripe for technology development and set clear goals for their development. This, in turn, will create the clarity and focus needed to create product-oriented development pathways that will attract interest from organizations that can provide funding throughout the development process.

Brainstorming Session

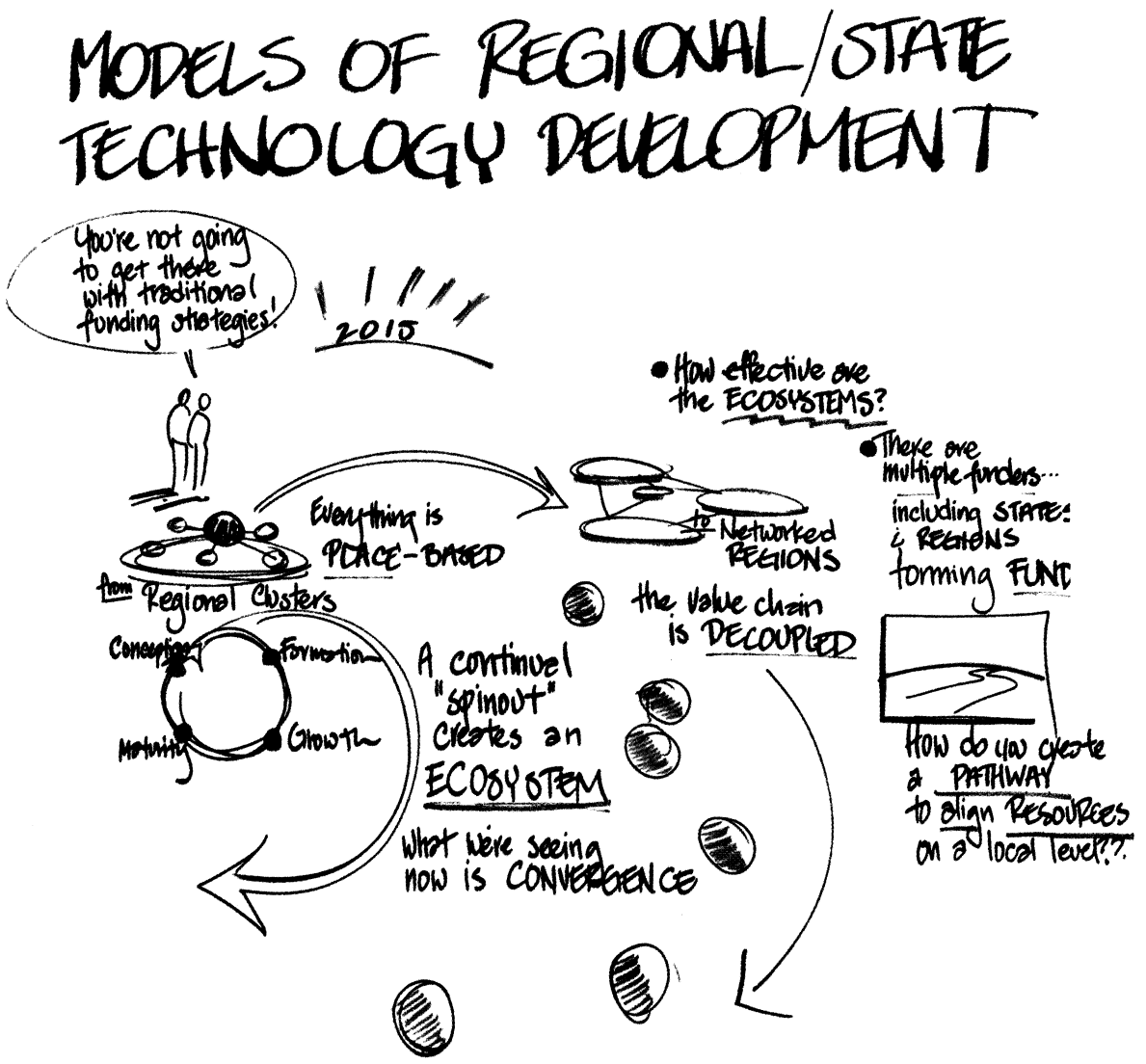
Mission Critical Barriers

Roundtable participants responded to the presentations by highlighting some of the major barriers that they felt would have to be overcome to speed up the advanced technology process development process for cancer and improve investment returns to those that invest in their commercialization. The lack of established technology goals and milestones, accountability for outcomes, and incentives for technology platform development has clearly hampered private sector investment. The lack of outcome "predictability" of new cancer agents in clinical trials leads to staggering economic costs and missed opportunities when these new therapies fail in Phase III trials. Thus, clinical trials sponsors from all sectors should be important targets for the development of new risk-lowering partnerships. Other Roundtable participants focused on impediments to development that have evolved in NCI and NIH-sponsored research—and are often just accepted as part of the culture. Included among the formidable impediments to commercialization cited by the group were the lack of cross-disciplinary technology development teams, difficulty in obtaining publicly supported data sets, confusion and delays incurred by highly variable intellectual property management strategies across the academic sector, and the lack of a real mandate for health-related development by Federal funders of basic research. (See Appendix 1.)

Panel 2

Models of Regional/State Technology Development that Overcome Barriers and Enhance Advanced Biomedical Technology-Based Economic Growth

With the 2015 challenge goal as background and keeping in mind the challenge presented by Panel 1, the conversation turned toward innovative multi-sector models that address some or all of these challenges. Several panels specifically presented a range of State and regional government, business, philanthropic, academic, and other models that have a history of aligning and optimizing the use of their resources to foster innovation and entrepreneurship. These models generally yield far more product milestones and economic returns than could possibly have been achieved by



an isolated, single entity. Time after time, these collaborations have shown that the output from the whole is greater than the sum of the parts. Panel 2 initiated a discussion of models that addressed what it takes to bring the pieces together and optimize their output in the State and regional settings.

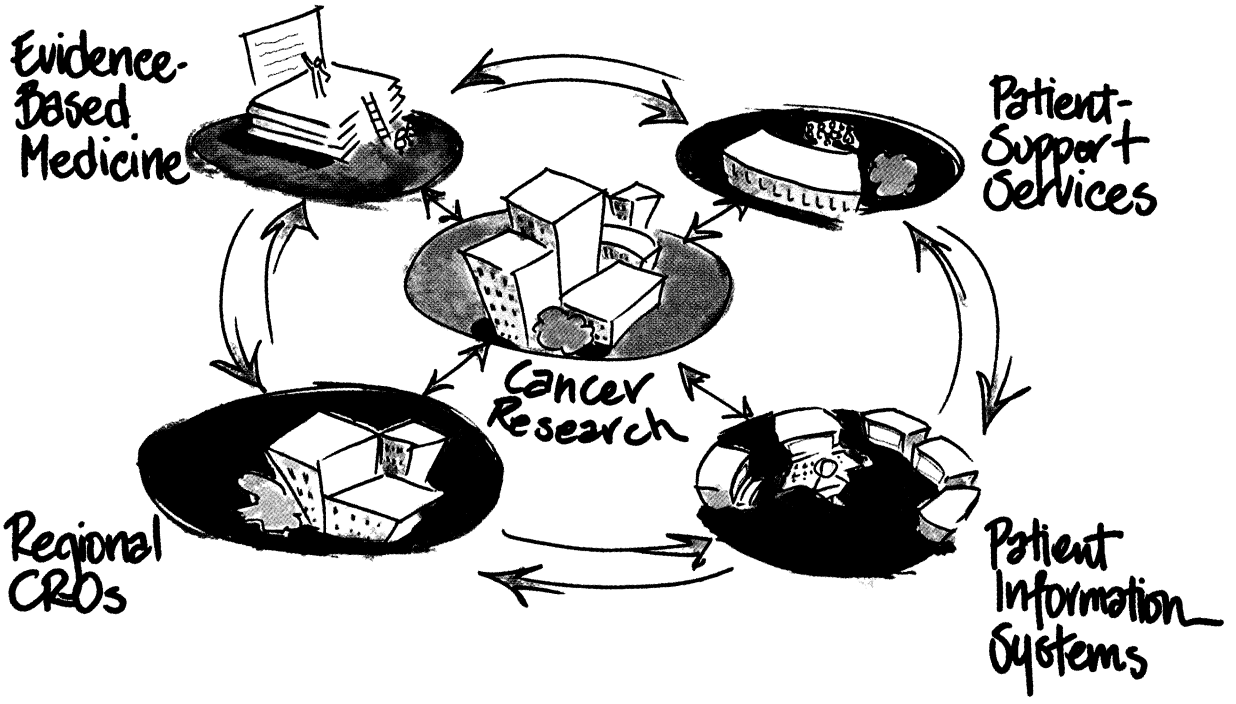
Mr. Richard Seline, Principal, **New Economy Strategies,** provided a framework and background for the Roundtable participants on State and regional models of innovation and entrepreneurship in the biotechnology arena. Panel 2 examined several successful case studies of State/regional technology development and innovation models. Mr. Seline focused his remarks on the ideal for these models—an economy-driven, "innovation ecosystem" that assembles from "clusters" of technology interests. This ecosystem is created within communities—it is "place based"—and begins with local suppliers of advanced technologies and services, which are usually academic medical centers or, in this case, cancer centers. In addition to the academic

centers, these networks may also include State and Federal agencies, the private sector, and other partners. Although these same resources may exist in many locations, often there is no strategy to align them. Given that there have been some real success stories, many regions are vying to be the next life sciences "supercluster." The process by which these "superclusters" evolve begins with the assembly of a varied set of stakeholders (e.g., investors, specialized services, health care services, academic institutions, and information technology) to determine how to leverage their specific assets. He stated his belief that some regions "innovate" better than others due to their unique abilities to bring together economics and science that progress through a cycle of development that moves from conception, formation, growth, and maturity. The critical aspects for the success of this "innovation cycle" include capabilities for knowledge creation, technology transfer, commercialization, and cluster/network formation. Mr. Seline believes that today, there are probably four or five regions in the United States that currently have a capability for "churning" through this innovation cycle. One output measure of the success is the dramatic growth in the number of small companies in these regions. Experts forecast that, in the future, these self-contained regional clusters will evolve into specialized networks that span geographic barriers and/or their traditional technology bases.

Mr. Seline posited that the NCI has many opportunities to leverage the capacity of cancer centers, research networks, and laboratory consortia. One strategy to enhance this leverage is to align these distributed capabilities to optimize Federal investment in these regions. In aligning these resources, it is important to consider that Federal funding for cancer research is also provided by the National Science Foundation, the DoD, and others and that many of these regions have formed their own venture funds for life sciences research. Alignment, driven by a combination of Federal, State, and regional investments, will support the convergence of network and systems into national "hubs and nodes" to support the development of advanced technologies for cancer—and their clinical deployment needed to achieve the 2015 goal.

The discussants in Panel 2 were executives from regional and State technology development groups with significant investment interests in cancer. Leaders from Research Triangle Park, NC, Philadelphia, PA, and San Diego, CA, presented key insights into these models. Roundtable participants heard about the strength of engaging multiple organizational partners—universities, medical centers, local and regional governments, and entrepreneurs—to create risk- and reward-sharing systems. In a sense, such regional cooperative models, when well executed, create a development "ecosystem" that by its nature fosters success in technology development as the unifying purpose for collaboration. Each of these models has a consistent history of leveraging NCI funding to create a venture-funded entrepreneurial core that is capable of bringing products through the late-stage discovery and early-development phases, which is often so difficult to achieve.

Dr. Frank Baldino, Chairman and CEO of **Cephalon, Inc.,** discussed an emerging innovation/entrepreneurship model in **southeastern Pennsylvania** that is focused on advancing discoveries from cancer research through development into commercialization. The Philadelphia area is a nexus of pharmaceutical and biotechnology companies, basic and clinical cancer centers, medical schools, and financial centers, with more patient beds and medical schools than any other region in the country. Leaders in the region were asked for recommendations on how to spend at least some of the state's tobacco settlement funds to leverage this unique core for economic development. The resulting plan used $100 million to create "greenhouses" that provide gap funding to early stage biotechnology companies. Funds are provided either as "seed funding" for promising startups or as matching funds for venture-funded companies.



Using this greenhouse approach, the Philadelphia region is building a Cancer Cluster Project (CCP) that has four components—evidence-based medicine, patient support services, patient information systems, and a regional contract research organization. The latter is built on the core cancer research efforts under way at the region's public and private institutions. Each of the four components receives a different mix of corporate, Federal, State, and philanthropic funding, and each links to the other through an interconnected network that aligns the interests of the public and private sectors. For example, the regional contract research organization, will provide centralized data collection and analysis capabilities and standards to link the major cancer treatment centers, universities, and hospitals to the private sector. This resource will streamline clinical research.

The CCP is also creating an evidence-based medicine institution supported by funders as diverse as health maintenance organization/third-party insurers and academia. The patient information services component is also funded by nontraditional sources, such as Lockheed-Martin. The goal of this initiative is the creation of an individual, portable "life card" that contains a patient's full medical record. The patient support services component seeks to increase the patient's knowledge about regional clinical trials. The overall goal of the CCP is integration of these services to enhance the quality of information for and about patients.

In the Piedmont region of North Carolina is a State model for biotechnology development with a much longer history. **Dr. H. Kim Lyerly,** Director of the **Duke University Cancer Center,** noted that the origins of **Research Triangle Park** (RTP) as a technology center arose from a goal to link North Carolina's State government, industry, and academia to specifically catalyze R&D that would complement activity in local major universities. This effort and their investments have paid off. In the ensuing years, investments by megacorporations such as IBM, Burroughs-Wellcome, and Glaxo, aligned with those of Federal R&D agencies, the U.S. Environmental Protection Agency and the National Institute for Environmental Health Sciences, have driven the "bioeconomy" of this region. The RTP is now a well-established ecosystem of technology development and is uniquely situated to leverage technology development among North Carolina's three NCI-designated cancer centers.

Regional investment firms play a key role in the life cycle and ultimate success of these technology models. **Dr. Ivor Royston,** Managing Partner of **Forward Ventures,** represented a **southern California** model where the increasing importance of advanced cancer technology development is his focus as a venture capitalist. Dr. Royston's firm develops early-stage biopharmaceutical oncology companies. In citing the remarkable growth of biotechnology companies in the San Diego area, Dr. Royston cited several key factors that have resulted in success. Having one institution or one person take a leadership role in championing and developing the technology is critical. This role is often filled by a clinical cancer center, with civic and political organizations stepping in to provide additional support. Successful State and regional development models are also able to secure multiple funding sources, including state and local governments and foundations that allow for creating needed pools of seed and venture capital. These seed and venture funds create an environment that further supports and fosters entrepreneurial activity. This is based on the scientific and technological discoveries and the subsequent intellectual property (IP) generated by investigators at the collaborating institutions. This, in turn, attracts interest from the broader venture capital community, which further encourages development activity in the region. Regional cooperatives can even drive clinical development by creating collaborations that can perform clinical trials on new chemical entities. This is a high-value activity, since it can be done in exchange for future payoff, which does not require that a company be formed to develop a single drug.

Panel 3

Innovative Nonprofit Models That Capture Technology and Leverage and Align Philanthropic and Other Resources to Optimize the Development and Commercialization of Advanced Biomedical Technologies (Incremental or Disruptive)

Building on the theme of models that leverage and align research infrastructure to accelerate the development of advanced cancer technologies, members of Panel 3 offered a range of perspectives on how to build the teams, interfaces, collaborations, and partnerships needed to succeed. In large part, these nonprofit organizations are acting as hubs that foster the multidisciplinary research, technology integration and collaborations that are essential where the study of complex biological systems is expected to yield the biggest payoffs for cancer. Representatives from three unique nonprofit organizations represented the many Roundtable participants from this sector by providing insights into their specific approaches to leveraging and aligning resources.

Dr. Leroy Hood, President of the **Institute of Systems Biology** (ISB), provided an overview of his institute's approach to capturing innovation and facilitating the development process for advanced biomedical technologies. The organization was founded with the intended purpose of shifting the research paradigm (especially cancer research) from single-focus reductionist research to new multidisciplinary and transdisciplinary models that can understand and ultimately intervene in complex living systems. The ISB's research focus is to define and manipulate the biological networks of life and, in doing so, become a user and developer of advanced biomedical technologies. Dr. Hood discussed the substantial impact that microfluidics, nanotechnology, imaging tools, and biocomputing are having on creating new technologies for cancer and all of health care. He cited the need for multiparameter diagnostic technologies, which is a major force at ISB. To further enable technology development, venture capital support has been engaged to support an environment that fosters the formation of early-stage biotechnology companies. Dr. Hood called for new mechanisms to support systems-oriented research and appropriate reward structures to build the teams that are needed to perform systems biology research. He closed by reenforcing the value of a systems approach to cancer—to both enable the required research and develop the advanced technologies needed to achieve the NCI's 2015 goal.

There is little doubt that new and novel approaches to the development of advanced technologies will be needed to overcome cancers that occur in low frequencies yet have devastating outcomes. **Mr. Steve Case,** Cofounder of the **Accelerate Brain Cancer Cure** (ABC^2) and the **Case Foundation,** discussed the strategies that ABC^2 is pursuing to accelerate progress against brain tumors. This organization supports translational research by providing resources to investigators to screen molecules for therapeutic activity and follow-on development. They also assemble teams of scientific experts to collaborate on finding the solutions to scientific problems. In

looking at the current systems problems that are hindering progress against cancer, Mr. Case drew upon his business experiences during the exponential growth of online computer services. He cited the key role government played in that success by enabling the Internet to connect with the existing telephone infrastructure circuitry. In reflecting back on his early interest in medical research, Mr. Case said he continues to be surprised by the lack of a connected infrastructure among cancer researchers, clinicians, and companies—indeed all of the players who can contribute to conquering cancer. In defining what changes are needed to accelerate cancer research, he noted that we have a lot of train cars, "but no connecting tracks;" nor do we have a structure to leverage the collective knowledge base that already exists in cancer today. Building common technology platforms and connecting all of the players would go a long way toward solving many of the problems inherent in the development and deployment of advanced technologies for cancer.

Mr. Leslie Michelson, Vice Chairman and CEO of the **Prostate Cancer Foundation** (PCF), cited several advances in prostate cancer research in the previous decade. The PCF, founded by Michael Milken has successfully developed and employed a range of rapid-response funding mechanisms and attracted substantial leadership to raise public awareness and bring attention from all sectors to prostate cancer. For example, the PCF has successfully provided input to national agencies such as the DoD and the FDA to ensure that their missions and goals consider prostate cancer. As a result of this leadership, especially the PCF's investments in biomedical research, a large number of talented researchers are now working in prostate cancer and share their results on an annual basis (the "brilliant string" concept). In addition, drugs such as Velcade® have derived from these efforts; issues of prostate cancer disparities are being addressed; lifestyle and nutrition are now a focus for prostate cancer research and delivery; prostate cancer tissue banks and databases that document genetic information are in place and/or in development; and international PCF-led collaborations are moving the field forward internationally.

As a result of these and other efforts, a collaborative effort among academia, government, and industry has produced a 50% increase in the number of prostate cancer drugs under development compared with five years ago, and the death rate from prostate cancer is declining. However, new challenges have emerged, including redesigning clinical trials to gain biological understanding of the disease and reduce trial length; decoding the heterogeneity of the disease; accelerating patient recruitment in clinical trials and making clinical trial data collection more efficient; and strengthening the bonds among academia, government, and industry.

Dr. Michelson suggested that the NCI place real emphasis on breaking down barriers in the regulatory area and caBIG could help. Furthermore, software applications must be developed, and the academic brain trust must be linked with industry to create a much more efficient and productive process.

Although technology commercialization strategies centered at major research universities is not a new concept, **Dr. Carl Gulbrandsen,** Managing Director of the **Wisconsin Alumni Research Foundation** (WARF), discussed a unique model that has taken a different approach. WARF has been a national leader in managing technology development through commercialization since its founding in 1925. The WARF exclusively serves the University of Wisconsin-Madison by patenting the discoveries and licensing these technologies to leading companies in Wisconsin and the United States and worldwide. Dr. Gulbrandsen cited several features of this technology development and commercialization model, including its independence from the university administration and capabilities of linking with philanthropy to sponsor high-risk, high-impact technology development. He stated his belief that this model was capable of achieving a great deal more in the future.

LUNCHEON PRESENTATION

Mr. Michael Milken—*Accelerating Medical Solutions*

Mr. Milken, Chairman of the Prostate Cancer Foundation (PCF) and Center for Accelerating Medical Solutions, presented the Roundtable with some important ideas on how to apply novel funding models to cancer research to simultaneously increase the probability of technology development success and ultimately the rate of financial return. He also called for fundamental systems changes related to the way in which the Nation conducts biomedical research and development activities.

What transforms societies? Technology advances, including those that have produced stunning changes in life expectancy. Over the course of the 20th century, worldwide life expectancy more than doubled, whereas life expectancy in the United States rose from 50 to 77 years—an increase of 54%. In 1900 one of every five infants born in the United States died before age 5, a tragedy that 16 of our Presidents have experienced. These incredible advances are largely the result of technology development, ranging from improved sanitation to the development of antibiotics.

Over the past 30 years, new technologies have had a profound impact on everyday life. Financial technologies have dramatically lowered the cost of mortgages, increased the ability of companies to raise money for research and development, and even changed the way we pay our bills. The exponential growth in computing power ushered in the personal computer revolution with its myriad impacts. In biomedicine, technological advances have cut the cost of sequencing a gene from over $100 million per gene in 1974 to $6 today. By 2013 that cost should drop to $0.03 per gene, a rate of improvement that exceeds Moore's Law. But cancer is one area in which the dramatic effects of technology improvement have yet to be significantly felt. This shortcoming is demonstrated by the fact that more people die of cancer annually than the total number of Americans lost in all the wars in the 20th century. We must, said Mr. Milken, focus all of our resources on bringing the power of advanced technologies to bear on cancer.

How might we achieve this goal? To start, he asked the Roundtable audience to consider the remarkable increase in global wealth creation that has occurred over the past 18 months, in which global equity markets have risen by one-third. In the United States alone, the largest 18 companies have increased their market capitalization by over $1.1 trillion. This rise has been even sharper among technology-driven biotechnology companies compared with their more established pharmaceutical company peers, demonstrating the impact that technology can have and the potential for returns to investors who put their money to work in fields such as biotechnology. He said the only threat to the United States' leading position in such technology-driven fields is the dramatic rise in engineering and other technical graduates abroad, particularly in Asia. China alone is turning out over three times as many engineering school graduates as is the United States.

Mr. Milken then discussed some of the key components of how to make major advances in the fight against cancer. First, we must internationalize the war on cancer, which is happening to some extent, but which should be pursued more aggressively. Investing more in cancer research is critical; eliminating deaths from cancer would be worth $46.5 trillion dollars, a potentially astronomical return on investment. Training and recruiting world-class scientific talent must also occur, something that the Prostate Cancer Foundation has emphasized in its efforts. It will also be critical to mobilize patients and their families as active participants in the war on cancer. An organized effort in this area could provide critically needed support for plans to establish an international database of patient medical records. To accomplish this we may need some legislative action to allow patients to choose to be part of a large database development effort for cancer vs. privacy protection. The payoff for such a database would be better information and incentives for patients to join clinical trials. All of these efforts would dovetail nicely with the NIH Roadmap for Medical Research. Finally, we need a "Framingham" lifestyle-type population study for cancer.

He noted that systems changes must also occur, including the creation of new tax policies that encourage biomedical research and development. To accelerate development, we must ensure that medical students and residents receive appropriate training. To speed the development of new cancer interventions, we must increase incentives for patients to participate in clinical trials, streamline the regulatory process through the development of surrogate endpoints, and better define what is needed for approval. We must allow contemporary science to drive a new and flexible clinical trials model. Industry must become a major player in all aspects of conquering cancer." To facilitate this engagement and enable key phases of the development cycle, we must lower risk by providing incentives such as extending the period of patent protection for novel drugs and diagnostics and strategically provide a range of Federal support mechanisms and new partnerships. Mr. Milken emphasized that it is critical that we harness the power of genomics, proteomics, and other advanced technologies to create new diagnostics and therapeutics for cancer with a sense of urgency.

Finally, he spoke of the need for better alignment of for-profit, academic, government, and foundation resources to conquer cancer In particular, he noted that the enormous increase in wealth that has swept the world over the past decade, and in particular over the past 18 months, has created a new generation of potential philanthropists, who are yet to make their mark. Cancer will be important to many of them. One strategy to accomplish the alignment we seek is to couple foundation funds to entrepreneurial activity. We should seek to create "virtuous" cycles of support for research and development tied to a return on investment. We also must provide more innovative funding models for the development of advanced cancer technologies that include venture capitalists, regional entrepreneurial development, and philanthropic models. Finally, we should seriously evaluate the In-Q-Tel model in a demonstration project. Combining a "virtuous" cycle to create return on investment with innovative new funding models will accelerate the development of advanced diagnostics and therapeutics that we need to reach the NCI's 2015 goal.

DAY 2

Focus on solutions—recommended actions by all sectors to accelerate the development of advanced technologies to conquer cancer

Mr. G. Steven Burrill—The Future Isn't What It Used to Be: What It Will Take to Identify and Develop the Needed Disruptive Advanced Biomedical Technologies

Mr. Burrill led Roundtable participants through the realities that face the biotechnology sector in the immediate future and longer term. Venture capital investments have been the defining source of support for biotechnology since its inception; but there is little doubt that years of market volatility have left their mark on this potentially high-value industry. In 2000, $32 billion was invested in biotechnology, and that level has decreased to $12 billion in 2001 and $10 billion in 2002. Thankfully, there were signs of improvement in 2003, with $16 billion invested. The biotechnology market is somewhat unique in that what drives the market is its passion for cutting-edge discovery, which often means that the "customer" may not see a product for 1 to 15 years and often not at all.

The biotechnology industry is fundamentally related to, and often contiguous with, centers of academic excellence. Several regional biotechnology initiatives have emerged during the past few years, and biotechnology is one of the top-priority investment areas for many State and regional economic development programs. Forty-one States currently have biotechnology development programs, and States such as Pennsylvania, Michigan, and Arizona have used money from tobacco settlements to fund biotechnology initiatives.

Looking ahead as the sequencing of the human genome is completed, enabling technologies such as genotyping, single-nucleotide polymorphisms (SNPs), functional genomics, and proteomics will define discovery and development, leading to an era of "personalized medicine." There is a clear improvement trend in biotechnology. The number of life sciences products in clinical trials is increasing, as are approvals, products, revenues, profits, and market capitalization, but the capital that underlies the industry remains volatile. The regulatory process continues to be highly unpredictable and results in a large number of expensive failures for the industry. The lack of an American public that is educated on key science policy issues, such as cloning, stem cells, and gene therapy, is also a major barrier to the future development of biotechnology in the United States.

In reviewing financing for the industry, he highlighted the fact that government spending has increased for defense and bioterrorism-related health technologies where the market needs diagnostics, vaccines, and drugs. Worldwide, the biotechnology enterprise is a $50 billion industry. If one compares the combined

value of Pfizer and Merck with the whole of the biotechnology industry, there is clearly a misalignment of investor resources. Pfizer and Merck combined have about 35 products on the market and twice that number in development, and their combined 2003 revenue was approximately $85 billion. By contrast, the biotechnology industry has 155 drugs on the market, more than 370 are in clinical trials or awaiting FDA approval, and the aggregate revenues of the entire biotechnology industry for 2003 was only $45 billion. This example demonstrates both the extent to which the biotechnology industry is currently undervalued and its promise for the future.

Analysts generally agree that biotechnology fundamentals are strong; however, the industry faces a number of formidable challenges, including uncertain volatile capital markets; complexity of the science and the diseases targeted, intellectual property (IP) issues; advanced healthcare technology development in the face of rising costs; and engagement and acceptance of the science by the public. The discovery, development, and commercialization of advanced healthcare technologies is embedded in a complex system that includes stakeholders that range from academic scientists to government payers to regulatory agencies, and this system must change. For example, R&D investments by the large pharmaceutical companies have not resulted in an increase in new drug approvals, producing an apparent innovation gap that may be addressed by the biotechnology industry.

Mr. Burrill noted that breakthroughs such as systems biology and "theranostics" will drive the biotechnology industry in the next few years. Systems biology will require new resources from a wide array of areas and new sectors (e.g., computing and bioinformatics, nanotechnology). "Theranostics"—combined diagnostic and therapeutic platforms that are interdependent—will change the way medical products are developed and marketed and eventually the way medicine is practiced. Biomarker-based diagnostics will ultimately change the "blockbuster" drug model, drive a new reimbursement and business model, and shift the current disease treatment paradigm toward attaining and sustaining wellness. In addition, diagnostics will enable personalized medicine through target identification and combating adverse drug reactions.

Interestingly, oncology currently represents the largest therapeutic area being pursued by the biotechnology industry. Investment in oncology has grown because of a seemingly favorable regulatory framework (e.g., fast-track and orphan drug protection). However, venture capital companies are wary of the area due to looming price controls for oncology drugs and the slowness and unpredictability of the regulatory process. Therefore, although there are unprecedented opportunities to develop advanced biomedical technologies for cancer, public and private capital markets are driven by short-term results, and there is insufficient venture capital funding dedicated to cancer.

Mr. Burrill left Roundtable participants with specific suggestions for changes that all sectors could implement that support reaching the 2015 challenge goal, including:

- Promote SBIR grant availability for venture-capital-backed companies;
- Create government-sponsored venture capital organizations for cancer (e.g., In-Q-Tel) for cancer technology development;
- Address the late discovery to early development gat—increase the rate of technology transfer from the laboratory to development;
- Design funding vehicles to advance drugs in trials rather than just create companies;
- Promote R&D credits for investors;
- Partner with the FDA to increase efficiency (e.g., decrease cycle times);
- Support developments of theranostics packages; and
- Increase staffing for the FDA to support pre-IND meetings with biotechnology companies.

Panel 4

An "Outside-the-Box" Federal Model to Identify and Accelerate Advanced Biomedical Technologies—In-Q-Tel

Several Government agencies have created innovative technology development models that facilitate the funding of milestone driven technology development programs in a timely fashion. The Central Intelligence Agency (CIA), the DoD, and most recently the DHS have each created models that function more like venture capital models than typical programs from government funding agencies. The CIA, for example, created In-Q-Tel, a stand-alone venture capital entity, to fund technology development deemed critical to its mission. The DHS Homeland Security Advanced Research Projects Agency (HSARPA), modeled after the DoD Defense Advanced Research Projects Agency (DARPA), funds contracts for mission critical technologies. Each of these specialized programs uses contract funding mechanisms to support research that combines project management with the timely delivery of milestones. These models could be highly appropriate to accelerate the development of the advanced cancer technologies needed to achieve NCI's 2015 goal.

Mr. Richard Seline, **Mr. Richard Johnson,** Senior Partner, **Arnold & Porter,** and **Mr. David Smith,** Vice President, **Technology Futures,** provided an overview of the history and operation of CIA's In-Q-Tel model. The CIA developed this model to facilitate partnering with the private sector to ensure the availability of the advanced

LUNCHEON PRESENTATION

Dr. Jane Alexander—*The Role of HSARPA in Developing Advanced Technologies for Homeland Security*

Dr. Jane Alexander, Deputy Director of the Homeland Security Advanced Research Projects Agency (HSARPA), provided a provocative and informative view of the Agency's approach to developing advanced technologies for homeland defense. She gave an overview of the newly formed agency, which uses competitive, project management-based, funding mechanisms to fund targeted research aimed at creating specific (urgently needed) products to achieve the mission of the DHS. As the external funding arm of DHS's Science and Technology Directorate, the HSARPA focuses on achieving milestones and specific deliverables. Specifically, these mechanisms are used to fund R&D activity that is designed to produce a needed product over 3 years or less. The HSARPA is in its first year of existence and was created along the lines of the model established by the Defense Department's Defense Advanced Research Projects Agency (DARPA).

To identify projects that would be appropriate for this type of funding, the HSARPA holds frequent meetings with both researchers and "customers" such as the U.S. Coast Guard and Transportation Security Administration. These meetings facilitate matching specific areas of basic research that have reached a point of promise to create a needed product using a project management-style approach. Once the need and high-likelihood scientific approaches are identified, the HSARPA puts out a preproposal announcement asking for interested R&D groups to prepare a white paper that is reviewed to identify potentially successful groups. This review is followed by a formal Request for Proposal and review process. HSARPA program managers usually provide input to guide the development of these full-scale proposals. The HSARPA prefers that proposals come from collaborative teams.

The HSARPA selects the most promising two or three proposals to receive seed funding, which allows the selected teams to begin development work on a clear timetable. Following a specified time period, the HSARPA reviews the progress of each team and selects one team to receive full funding in order to produce the defined product—again on a strict timetable. Throughout the process, HSARPA program managers work closely with the selected team to ensure that milestones are met. Perhaps of more importance, these programs managers help the selected team overcome technical problems by identifying suitable off-the-shelf technology that could solve the problem or by developing links to additional experts who may also offer solutions. The NCI's Unconventional Innovation Program (UIP) is similar in this aspect of HSARPA's "helping hand" approach. In upcoming months, the HSARPA plans to solicit proposals for a broad range of technologies for biodefense. Dr. Alexander offered to continue to work with members of the Roundtable to explore collaborations with her agency.

technologies needed by the intelligence community. In-Q-Tel was designed to search for and fund cutting-edge technologies, develop new ideas and products through collaborative partnerships, and incubate the development of innovative ideas and tools. This is an "out-of-the-box" model, since like the NCI, the CIA was limited by Government restrictions in its authorities to form partnerships with the commercial sector. In-Q-Tel faced many early challenges, including a slow start for the program, congressional inquiry into oversight, management of funds and performance, investor and collaborator concerns about loss of IP rights, and shared ownership with the CIA (i.e., the "black box" nature of the agency and the fact that technologies could limit commercialization potential). In-Q-Tel uniquely combines the strengths of venture capital, R&D, Federally-Funded Research and Development Centers (FFRDCs), DARPA mechanisms, Advanced Concept Technology Demonstrations and a National Medical Technology Testbed. By interfacing with these communities, In-Q-Tel can pursue an aggressive strategy to define and meet market needs with an adaptable business models.

In-Q-Tel offers the NCI a model that aligns its activities with needs of the marketplace through strategies that promote development and commercialization and leverage third-party funds. Because In-Q-Tel is controlled indirectly by the CIA, it has attributes that are typically found in stand-alone (generally private) organizations. The Panel offered that In-Q-Tel might serve as a useful model for cancer technology development as it:

- Possesses a versatile and broad toolbox for business transactions, including grants, competitive mechanisms, and sole-source contracts;
- Operates as a catalyst and facilitator to stimulate collaborative activities;
- Provides flexibility that facilitates alignment with innovation ecosystems;
- Increases the information "bandwidth" through interface with other venture capital model programs;
- Provides guidance and models for addressing intellectual property issues; and
- Offers an agile, solutions-focused, output-measured, and innovative business model that could become self-sustaining over time.

Like cancer, In-Q-Tel must reduce cycle times to achieve its technology goals. By directing finances toward the gap between fundamental research and early-stage development, this model may be well suited to address this major barrier in cancer technology development.

Panel 5

Putting the Models to Work: Optimizing and Accelerating the Development of Nanotechnology for Cancer

Having analyzed a variety of technology development models, the Roundtable participants explored a case study of an emerging field that promises to make a substantial impact on cancer. Sharing with the participants their vision of how nanotechnology development for cancer could be accelerated were three national leaders: **Mr. Scott Donnelly,** Senior Vice President for Global Research and Chief Technology Officer of **General Electric, Dr. James Heath,** Professor of Chemistry, **California Institute of Technology,** and **Dr. Mauro Ferrari,** Special Expert in Nanotechnology to the **NCI** and Associate Vice President, **Ohio State University.**

Consistent with discussions throughout the Roundtable, Panel 5 examined the potential of nanotechnology and advanced imaging to be transformational for the early detection, treatment, and prevention of cancer. Nanotechnology has the potential to be a major force in driving a strategic inflection that will contribute significantly to the achievement of the NCI's challenge goal. Diagnostic imaging that

depends on materials sciences to develop the probes needed to interrogate systems at the nanoscale level could well be transformational by providing the technology needed to understand and visualize cancer processes in terms of function at the molecular level. Understanding function will enable both characterization of cancer and new diagnostic strategies. Mr. Donnelly emphasized that making this transition will require highly specific, targeted contrast agents that necessitate the development of amplification factors. In addition to imaging, the panel identified other highly promising areas for nanotechnology application in cancer, including multifunctional drug delivery and microfluidic systems for protein measurement and quantification.

Dr. Heath utilized some of the model technology development programs featured in the Roundtable to discuss projects that could fit these models. The goal of the collaborative group he described is to measure and quantify specific components in a small amount of a body fluid, perturb the system, and measure changes in real time. Currently, promising nanodevices are being tested in mouse models, but new strategies are in development to translate results from bench to bedside. Dr. Heath described the current **Nanosystems Biology Alliance,** a collaborative technology development model that includes the Institute for Systems Biology, the University of California, Los Angeles, and the California Institute of Technology. The Alliance is driven by the fact that for cancer time is critical, and progress is needed with a sense of urgency. Intellectual property issues have been resolved via agreements. The Alliance has set milestones and fully expects that some of these technologies will progress to clinical testing within a few years.

Dr. Ferrari pointed out the complex problem of cancer heterogeneity and associated variability in responses among patients presents significant challenges for evaluating nanotechnologies. For 10 years, liposomes, which are early-generation nanotechnology agents, have been used in the clinic. Yet optimizing the deployment of these early nanotechnologies has proved to be significant. Intellectual property is a major barrier that must be addressed for cancer to optimally benefit from the power of nanotechnologies. Because ownership of various components of the system often rests with different parties, it is likely that progress in the development of needed collaborative agreements will be slow. However, the NCI has the ability to bring component technologies together to produce nanotechnology-based diagnostic or treatment platforms for cancer. In addition, the NCI can lead an effort to standardize nanotechnologies for screening and create large combinatorial matrices that will enable the evaluation of thousands of potential cancer therapeutics.

Panel 6

Can America's Cancer Centers Serve as Major Vehicles for Capturing, Developing, and Commercializing Advanced Cancer Technologies?

The NCI's national network of 60 NCI-designated cancer centers is home to most of the vast array of cancer research being conducted today. These centers generate the majority of laboratory discoveries and technology that become the basis for cancer drug development that is carried out by the private sector. As such, cancer centers play a critical role at the "front end" of the drug discovery process—and now more often also in early development. The importance of this "engine of discovery" to the development of new cancer targets, and sometimes lead molecules has been reenforced in recent years through the commercialization of new agents such as Herceptin® and Gleevec®. The research mandate of clinical cancer centers and access to cancer patients makes them a powerful source for the design and performance of cancer clinical trials. These centers are also important in the conduct of postapproval optimization trials that ultimately determine the clinical utility and broad patient benefit of any given anticancer therapy.

Dr. John Mendelsohn, President of the **MD Anderson Cancer Center, Dr. Jonathan Simons,** Director of the **Winship Cancer Center,** and **Dr. James Willson,** Director of the **Ireland Cancer Center** presented their views on the role of cancer centers in optimizing and ultimately accelerating advanced technology development for cancer. They pointed out that cancer centers are key to leading change in training scientists and physicians in mission-oriented, collaborative research. Already, some of the most innovative cancer centers are leading drug and diagnostic development efforts by providing seed funds to move promising technologies forward and by creating good manufacturing practices (cGMP) level facilities and other shared technology core resources. These state-of-the-art capabilities enable investigators to pursue development goals that lower the risk to the private sector and improve the likelihood that the technology will be licensed. The panel pointed out that their institutions are well known within their local communities and can serve as vehicles for the NCI's message. These centers can drive the collaborations and partnerships needed to accelerate progress toward the 2015 challenge goal. In their discussions with Roundtable members, participants pointed to several key issues that would serve to improve the ability of cancer centers to leverage their capabilities in technology development. These included creating novel training awards for young scientists who are interested in technology development and formal cross-disciplinary training and extending career development opportunities to allow students to train in pharmaceutical and biotechnology companies and vice versa.

Brainstorming Session

Identifying and Removing Barriers to Technology Development

Roundtable participants engaged in a rapid-fire brainstorming session to discuss technical, social, clinical, regulatory, and financial barriers that impede progress toward the 2015 goal. One of the important outcomes of this brainstorming session was the acknowledgment that although these barriers are generally understood, there is a lack of leadership to establish goals, develop standards, and align technology development capabilities across sectors to remove these obstacles. If this is not corrected, the Nation will be unable to seize on the transformational post-genomics opportunities to accelerate progress against cancer and achieve the NCI's 2015 goal. The barriers identified by Roundtable participants are highlighted as follows:

Regulatory Barriers

- State-by-State differences in reimbursement for advanced technologies.
- A regulatory process that is in effect a disincentive to collaboratively test multiple agents.
- No well-defined mechanisms or provisions that would allow patients to opt out of privacy act and Health Insurance Portability and Accountability Act (HIPAA) for the sharing of clinical data.
- Unpredictability of the regulatory process for anticancer agents.

Economic Barriers

- There is an expensive period from late discovery to early-stage development that is too long and too high risk to attract needed investment.
- Access to capital for cancer therapeutics and diagnostics is poor in light of less risky opportunities in other disease areas.
- Intellectual property holders are often unrealistic in their expectations for financial reward, thereby limiting partnering capabilities.
- Little interest exists among venture and investment communities to fund diagnostics development.

Scientific Barriers

- Methods are needed to "fingerprint" tumors based on genes and proteins and to do so in a high-throughput capacity.
- Difficulty exists in translating our understanding of cancer heterogeneity into new interventions.

- There is a poor "system" by which scientific findings are communicated based on non-standardized data formats, which limits the ability to mine the data.
- There is an unmet need for a coordinated and broad biomarkers discovery and validation strategy for early detection and preemptions of cancer.
- There are no platforms for real-time data exchange and analysis.

■ **Cultural/Structural Barriers**

- Lack of entrepreneurial culture in many academic institutions provides limited rewards for those who do have entrepreneurial drive.
- Disincentives exist to cross-disciplinary collaboration and inter-institutional collaboration.
- There is a non-uniformity of policies and practices for collection and access to critical biospecimen and clinical data to facilitate technology development.
- Inconsistent IP approaches and unrealistic financial return expectations discourage progress.
- Industry structure and business models do not match the need for combination therapies and diagnostic-therapeutic combinations.
- Orientation of academia toward reductionism does not fit with the current view that cancer is problem of systems biology.
- The reward system in academia is not oriented to patient outcomes.

In addition, given the desire to identify concrete goals and recommend actions to surmount some of these barriers, the Roundtable prioritized a wider range of barriers, with four specific barriers selected for further analysis. The complete list of ideas used to stimulate discussion and develop action items is provided in Appendix 2.

Roundtable Action Items

Participants met in four thematic group discussion sessions that were charged to develop specific goals, near-term, and bold/audacious strategies for meeting those goals and metrics to judge the success of such efforts. These strategies were presented and discussed by the entire Roundtable (see Appendix 3). The following summarizes these discussions:

- **Building Cross-Disciplinary Collaborations.** Major breakthroughs in cancer will require an integration of knowledge about the fundamental processes that define cancer and their interactions. The group agreed that many of the major achievements in innovative technology development will come through a systems biology approach to understanding and conquering cancer. This approach will ultimately reduce the time required for the development of more effective, advanced interventions to detect, prevent, and treat cancer. The Roundtable suggested that two to three collaborative technology teams be assembled using a hub (leadership and management) and node (specific expertise and teams) model that are accountable in terms of deliverables and team performance. The teams should be supported at an appropriate level for five years and include support for training across disciplines, with a focus on clinical development to optimize interaction among team members. Teams should be region-based to improve interteam interactions and should be built with a goal of sustainability that would extend beyond the 5-year period of NCI support. Furthermore, the Roundtable recommended that funding mechanisms should take advantage of the innovative Federal models that target specific outcomes, such as the In-Q-Tel or HSARPA models. These mechanisms should employ a project management mechanism to increase the probability of reaching defined milestones.

  The goals are to reduce the time required for substantive progress and increase the efficiency and effectiveness of resources invested by developing a systems biology understanding of cancer. Such collaborative teams would have a central focus of leadership networked with nodes (specific expertise) that are accountable in terms of deliverables and the effectiveness of team members in achieving shared goals. Such teams will require cross-disciplinary training—and these new constructs could provide training to a broad segment of the cancer community. The quick strategy for meeting this goal would be to align existing resources and create two or three teams in 2004, with NCI jump-starting these efforts through targeted funding. More audacious strategies include having the NCI act as a catalyst, but moving to an In-Q-Tel or HSARPA model that would call for competitive, team-based proposals and allow the NCI to pursue a 5-year exit strategy in terms of Federal support.

Immediate first steps include designing a team framework with a focus on sustainability; launching the best models, with input from academia and industry and regional expertise; identifying champions; and providing NCI-supported, 5-year funding mechanisms. Project milestones would be assessed by project managers and success measured through a series of quantitative performance measures. These team science projects should also be evaluated on their effectiveness in attracting non-NCI funding from industry, venture capital, and foundations.

- **Bridging the Gap Between Late Discovery and Early Development of Diagnostics and Therapeutics.** To reduce the failure rate of new diagnostics and therapeutics entering clinical trials, with the resulting waste of financial and intellectual resources, the Roundtable came up with a series of interrelated goals. First, enroll 100,000 building to 1,000,000 patients in clinical trials and make the patient biospecimens and clinical outcomes data widely available. Second, develop 100 new mechanism-based IND applications, at least 50 of which will involve multiple new combination therapies (more than one moiety provided in a delivery system). Third, develop a "best-practices" standard for IND submission and conduct of clinical trials and establish a system for certifying the quality of clinical trial design. Fourth, construct new financial models for late-discovery/early-development activity of advanced cancer technologies that could be initiated through partnerships between venture capital and philanthropic organizations. Finally, revamp the SBIR program to concentrate on late-discovery/early-development activity and allow organizations with venture capital support to participate in the program.

  To reach these goals, the Roundtable recommended that the NCI build a project management structure to identify likely partners, create timelines for development, and establish quality standards. This structure should rely on successful Federal models for technology development. An advisory board drawn from academia and industry should be developed to advise on the development activities, including target identification and validation and prioritization of leads. Legislative action to increase time for patent exclusivity for oncology products (similar to the pediatric exclusivity provisions) should be pursued. The NCI should be given the authority to use innovative models to fund and direct late discovery/early development activity. A mechanism of financial risk-sharing among the venture community, private foundations, and an NIH foundation-like structure should be built and potentially facilitated by the NCI. The NCI should develop a novel screen that would "credential" potential interventions for cancer by providing information on systems effects, pharmacology, toxicity, etc. This activity could become part of a national resource for cancer drug development to provide standards and evaluate new advanced technologies. This would be a logical capability to include in the proposed NABTI—potentially located within a national "hub."

- **Developing Data Standards.** Improving the efficiency with which cancer researchers can compare and utilize data generated from both basic research and, all facets of development research and clinical trials would significantly speed up the range of research that will lead to novel therapeutics and diagnostics for cancer. Achieving this level of utility is hampered today by a lack of data standards that prevent data pooling and comparison. The NCI (potentially with industry partners) should convene a consensus meeting for defining the structure of standards to identify and validate biomarkers; report clinical data that can be widely used; and report molecular and structural data in a manner that increases access to and utilization of shared data. The standards should be defined and monitored through an organization that would assume responsibility for managing their use. The standards development effort should be global—perhaps coordinated through the Organisation for Economic Co-operation and Development. The NCI should foster change in the clinical and research communities to accept open-source access to data and link funding access to standards compliance. Finally, an NCI-led task force should be authorized to publish standards with a "seal of approval" for technology development.

- **Developing Cross-Cutting Technology Platforms.** Accelerating the development of novel therapeutics and diagnostics for cancer requires the identification and creation of cross-cutting technology platforms, such as nanotechnology, bioinformatics and proteomics. To meet this goal, the Roundtable suggested that the NCI take a leadership role in establishing development demonstration projects with a defined technology focus. One such project should be identified and operating within six months (e.g., biomarker development, nanotechnology, etc.). The NCI should create and disseminate initial standardized data sets for these platforms, provide the data collection tools needed to capture existing data in appropriate databanks. The Institute should also fund the development of a system for real-time monitoring of data sets based on systems that agencies, such as the DoD, NASA, and HSARPA have developed for this purpose. Finally, the NCI should drive the development and dissemination of standardized platform hardware and software and work with public and private sector organizations to establish a data framework to capture data from these specialized technology platforms. As a first step it is critical to inventory the biomarkers and platform technologies available today. It is also critical that the NCI convene a group of experts from academia and industry to identify the technologies that are needed to enable critical areas such as systems biology research.

Summary and Next Steps

The Roundtable discussants emphasized that the NCI alone cannot break through these barriers. The combined and coordinated efforts of all members of the Nation's cancer research and development and commercial enterprise will be needed. Participants noted that the NCI can facilitate a great deal of progress across all sectors by catalyzing and leading the transformational initiatives needed to optimize and accelerate the overall discovery, development and delivery continuum.

Interestingly, the Nation's cancer centers emerged from the Roundtable discussions as critical drivers for future advanced technology development. In this future, the cancer centers would increasingly become hubs for collaboration and technology development at the State and regional levels. Such regional efforts can serve as wellsprings of entrepreneurial development and attract capital from government agencies, venture capitalists, pharmaceutical companies, and foundations. New resource streams and mechanisms for technology development will be needed from all sectors; and support for basic/discovery research must continue to produce the laboratory advances and breakthroughs needed for the future. Participants looked to the venture capital investment sector to construct new approaches for capital- and risk-sharing collaborations. These could combine unusual funding sources such as nonprofit, health-related foundations that are just defining cancer related missions. The Roundtable encouraged the NCI and and/or other participants to bring together the financial and philanthropic sectors in a forum designed to craft project management strategies that would better align and leverage their resources to develop advanced cancer technologies. These collaborative financing models could serve as examples for other areas of biomedical research.

The Roundtable identified a number of actions that the cancer community must take to accelerate the development of the advanced technologies needed to meet the 2015 goal. Although the NCI is committed to catalyze and lead many of the required initiatives, the Institute cannot achieve the desired transformation alone. This must obviously become a broad multi-sector collaborative effort. Since the meeting, several participants have indicated their intent to take actions on some of the suggestions and recommendations that evolved from the panels and brainstorming sessions. On the basis of its deliberations the Roundtable also suggested a large number of follow-up cross-sector actions. The following list is not exhaustive, but details a few of those actions that are either underway or could be undertaken in the next few months:

- **All Four Priority Areas:** Many of the Roundtable participants indicated a willingness at the meeting (and subsequently) to work on solutions in one of the four priority areas identified. Conference calls will be arranged to discuss progress and seek ideas.

- **All Four Priority Areas:** NCI should continue to develop and articulate a compelling case for a national advanced biomedical technology initiative for cancer that can provide significant support to address all four of the mission-critical barriers identified by the Roundtable.

- **All Four Priority Areas:** Convene a working meeting of the venture capital and philanthropic communities – potentially with regions that excel in entrepreneurship/innovation and associated cancer centers. The goal of such a forum would be to identify and develop new funding strategies and streams for the development of advanced biomedical technologies for diagnosing and treating cancer. This could be convened by any one of the sectors or a combination of appropriate leaders, with the NCI as a collaborator in this effort.

- **All Four Priority Areas:** Assess the development strengths and potential role of the regional/state entrepreneurial/innovation centers and their relationship(s) to NCI's cancer centers. Convene a forum of key state/regional programs and associated cancer centers to develop "best practices" for technology transfer, early development models, partnerships, etc.

- **Developing Cross-Cutting Technology Platforms:** Set up a workshop comprised of the NCI, academia, private sector and other stakeholders as appropriate to define the technology platforms that would most rapidly accelerate the development of the new diagnostics and treatments needed to achieve the 2015 goal. This could initially proceed through focused workshops that define needs for specific initiatives; e.g., biomarkers; systems biology; etc. NCI plans to catalyze these workshops.

- **Bridging the Gap between Late Discovery and Early Development of Diagnostics and Therapeutics:** Convene a group of experts to address intellectual properties (IP) issues related specifically to biomarker-driven diagnostics development. The goal of such a forum would be to define new IP constructs that would facilitate the use of arrays of biomarkers for cancer diagnosis and therapeutic monitoring. This forum could be convened by key players in cancer diagnostics (e.g., cancer–focused foundations; members of the industry, etc.) and/or research leaders with an interest in facilitating the early detection of cancer and making the technologies broadly available. NCI would be an important contributor to such a forum.

- **Developing Cross-Cutting Technology Platforms and Building Cross Disciplinary Collaborations:** The NCI should explore new funding strategies for the development of advanced biomedical technologies. This exploration should draw upon the expertise of HSARPA, In-Q-Tel, and DARPA models. NCI was already in the process of investigating these models and will complete this exploration.

- **Developing Cross-Cutting Technology Platforms:** Depending on the outcome of the exploration of these new funding models, and NCI's access to these mechanisms, a pilot project(s) should be collaboratively developed that is focused on the development of advanced technologies to address a specific technical program (e.g., early diagnosis of cancer) in cancer research and development. This will depend on access to mechanisms and the availability of collaborative partners.

- **Developing Data Standards:** Convene a workshop of collaborative stakeholders to agree on a process to identify needed standards for cancer research and development and proceed to prioritize and create these standards. NCI will do some of this through its caBIG and other initiatives, but a more focused effort must include a range of a range of stakeholders.

- **Bridging the Gap between Late Discovery and Early Development of Diagnostics and Therapeutics:** The NCI and other stakeholders should explore the development of a screening process that could be broadly applied to "credential" new targets for cancer therapeutics development. This would include screens that provide information on pharmacologic and toxicological properties and impact on other systems. The NCI is exploring this concept as part of its development efforts and plans to hold a workshop on the topic later this year.

Appendix 1

Barriers Brainstorming. During the course of the Roundtable's brainstorming session on mission-critical barriers, participants identified a wide range of issues that limit the ability of the Nation's cancer research and development enterprise to more rapidly turn promising ideas into clinical advances. To help focus subsequent discussion and problemsolving activities, these barriers were grouped according to five overarching themes—scientific, cultural, structural, regulatory, and financial. A summary of this discussion is shown in the diagram below, which was prepared during the course of the brainstorming session. Overlaps between the areas are also readily apparent. At the end of the first day, Roundtable participants were asked to choose the four barriers considered to be the biggest hindrance to the field. Other choices are shown as red dots on the graphic below.



Appendix 2

Solutions Brainstorming. Prior to breaking up into working groups to consider the top four barriers prioritized by the Roundtable participants, the entire group engaged in rapid-fire brainstorming sessions to generate ideas for solutions. These were recorded to initiate thinking about specific solutions. A summary of the ideas generated is listed below:

- **Ideas for the Working Group addressing Cross-disciplinary Collaborations:**
  - Need mechanism to provide rewards for academic collaborators in clinical trials, which often does not happen
  - Dedicated funding for collaborative teams grant proposals
  - Scale up cross-disciplinary training in medical schools
  - Create meetings for cross-disciplinary interactions to ask the right questions
  - Gather and promulgate "stories" that show how others do this well
  - Need collaboration among funding agencies/foundations to share initiatives/integrate funding
  - Provide legislative authority to pilot new approaches and facilitate interagency collaboration
  - Fund video capabilities for labs to provide vehicles for easy, regular communication among labs/agencies
  - Create a detailed deliverables roadmap that will enable/accelerate collaborative efforts (in the way industry does for partnerships)

- **Ideas for the Group Addressing the Gap between Late Discovery and Early Development:**
  - Use government funds to provide venture funding through partnerships and loans
  - Explore launching development activities using new models
  - Share the financial risk with venture capital community
  - Provide input that will allow the FDA to better use results from research and development to appropriately change regulatory policies

- Use the SBIR program more creatively ($75 million at the NCI) and increase the use of SBIR funds to fill part of this gap (STTR also requires partnership between academic labs and private sector)

- Reverse the rule that SBIR funds cannot be used to support venture-backed companies

- Create a venture-like fund from philanthropic organizations to significantly accelerate development

- Require advanced identification of partners as part of grant funding processes for technology development

- Create a mechanism to allow better hypothesis testing in Phase I trials

- Significantly increase the value of the existing Rapid Access to Investigational Drugs (RAID) mechanism through goal-directed prioritization process

- Use newly identified "trustee mechanism" to allow national labs and other Government agencies to take equity positions and form partnerships in the development of entrepreneurial companies

- Create competitive Federal seed capital funds for advanced technology development

- Create a national policy on selling net operating losses

- Raise capital loss tax provisions for special circumstances (biotechnology investments)

- Coordinate core facilities in federally supported universities across the Nation to engage in early-stage development work

- Create a pool of funds from Federal (the NCI) and the States to move laboratory discoveries to a level that they could receive venture funding

■ **Ideas for the Group Addressing a Lack of Data Standards:**

- Generate large collections of data in targeted areas (through aggregation of databases) that will allow us to work on the creation of standards vs. working in a vacuum

- Harmonize international efforts

- Create a structure for identifying and eventually validating biomarkers that can be easily moved to industry—the Human Biomarker Project

- Create a national effort for biospecimens that standardizes collection, storage, access, etc.
- Identify data that the NCI could and should collect now and mandate a process and timeline for submission by all NCI grant recipients
- Partner with the National Institute of Standards and Technology or create a national bureau of biomedical standards that the NCI could lead
- Mandate and fund the development of standards, which will be expensive and must be done by Federal agencies
- Mandate disclosure of markers and data by grantees, which assumes a system of collection
- Mandate access to data, even to clinical data for approved drugs (could require legislative action)
- Distribute tools at no/low cost that are standards based
- Convene a national "congress" of all the players—the NCI, major data platforms, major tissue banks, data companies, etc. —to jump-start this effort and create standards

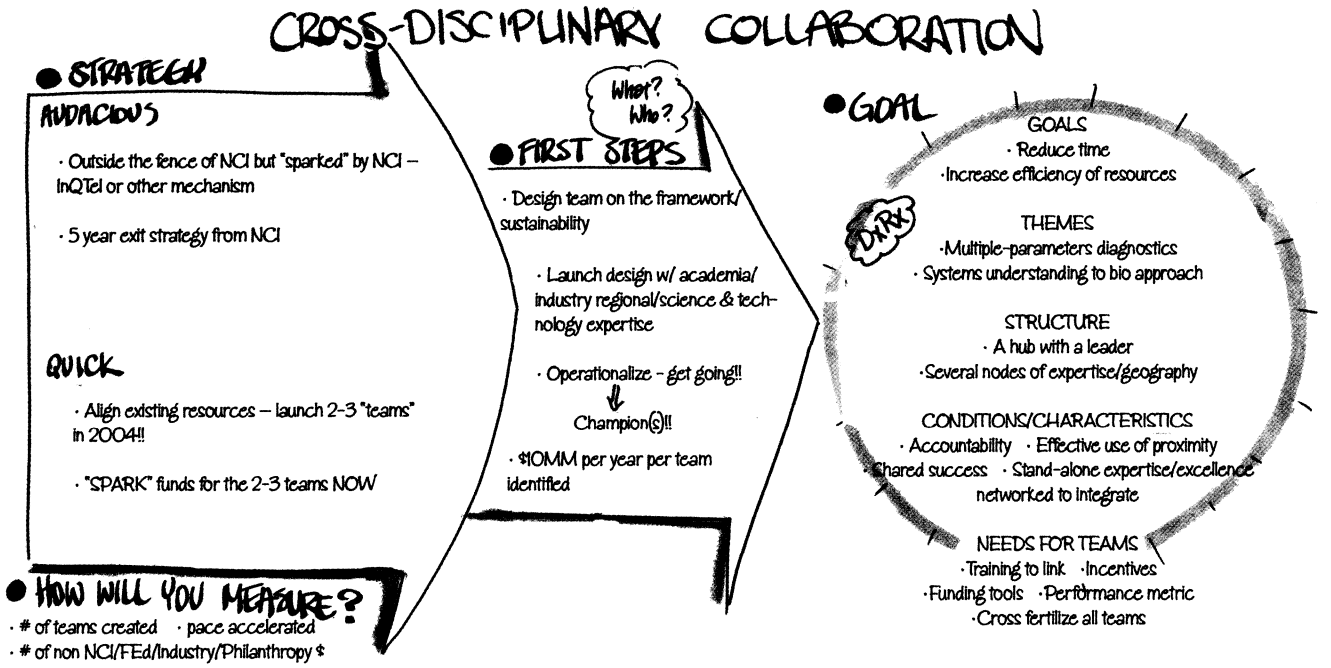
■ **Ideas for the Group Addressing the Need for Cross-cutting Technology Platforms:**

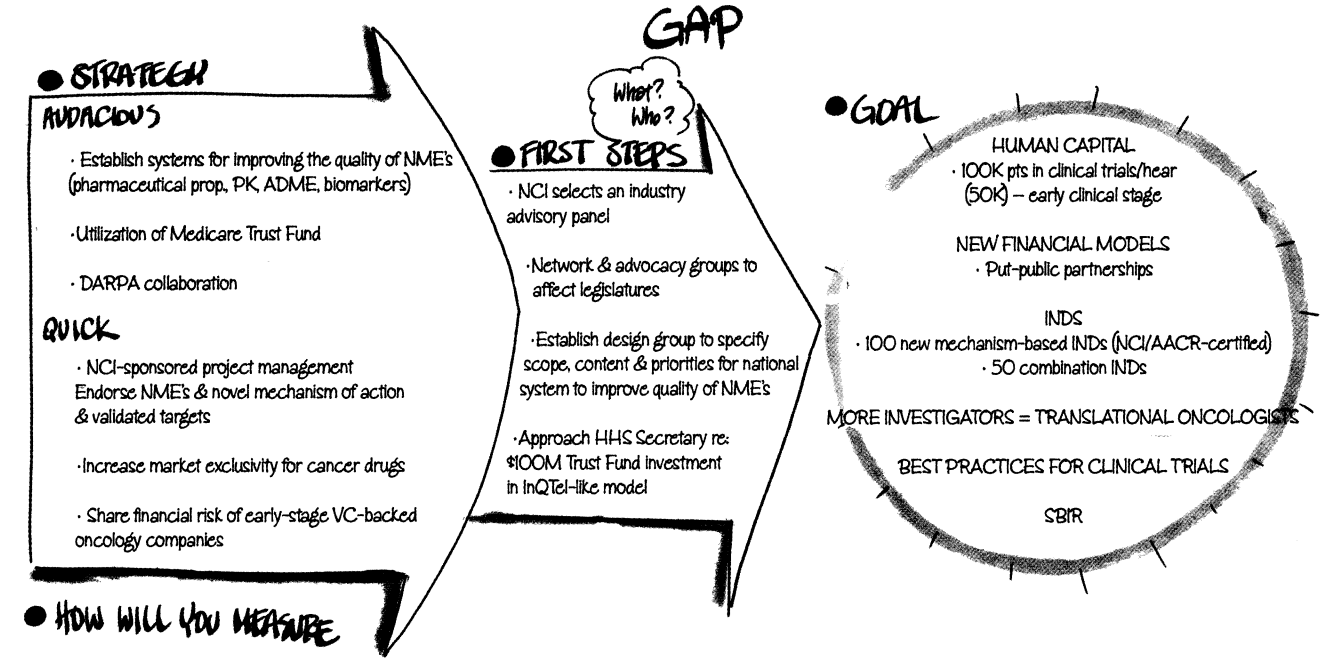
- Utilize the council of state biotech conferences, to both identify key stakeholders and provide needed political networking
- Create a platform that involves selected communities and physicians NOW to acquire the genomic/proteomic information needed
- Involve the national laboratories in this effort because that is what they do well
- Standardize novel emerging technology platforms in a neutral, centralized manner
- Define the advanced technology platforms needed for the 2015 goal
- Ensure that today's platforms are planned to achieve the 2015 goal
- Just do it! Stop talking and get on with assembling the players and structuring the solutions

- Inform the needed legislative action that would enable people to submit their medical records to the research enterprise—a Health Insurance Portablity and Accountability Act (HIPAA) bypass
- Create a platform that would seamlessly integrate clinical trials data with patient care
- Create an IP policy checklist that will be needed to enable reaching the 2015 goal
- Utilize political leadership at the State and national levels to encourage clinical trials participation
- Rebuild support in the capital markets for technology platforms
- Create an aggressive goal for NCI-funded demonstration projects in two or three areas of cross-cutting technologies within the next 6 to 12 months

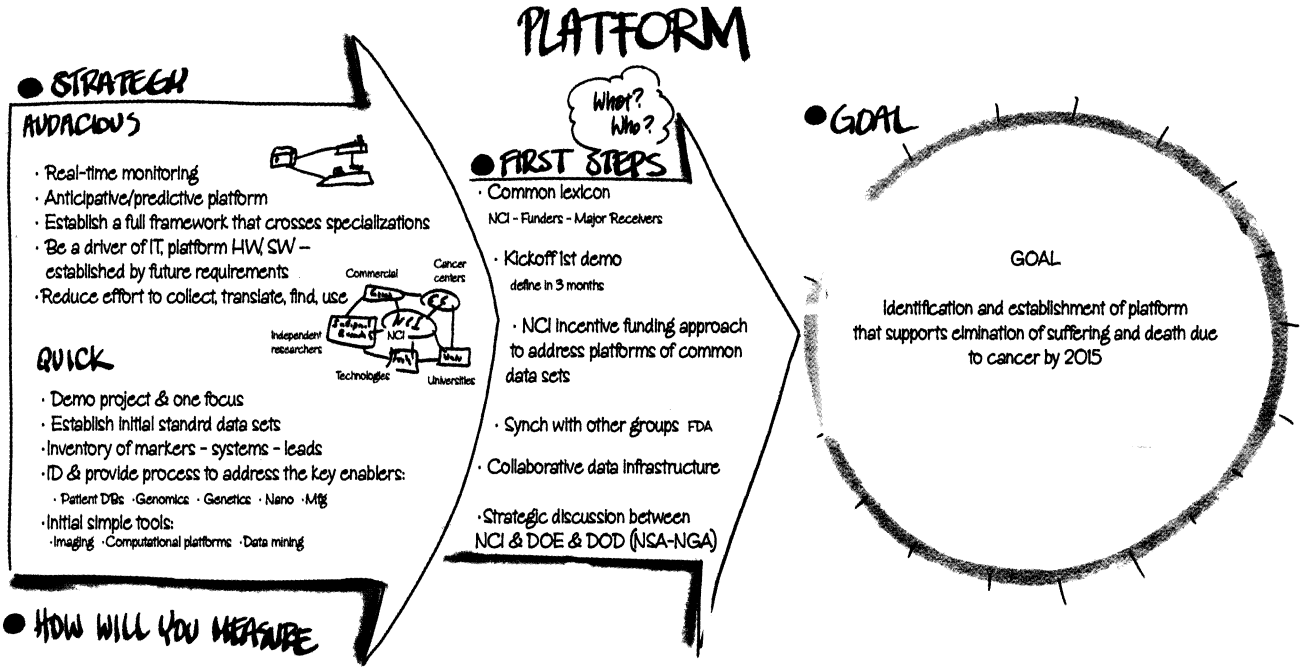
Appendix 3

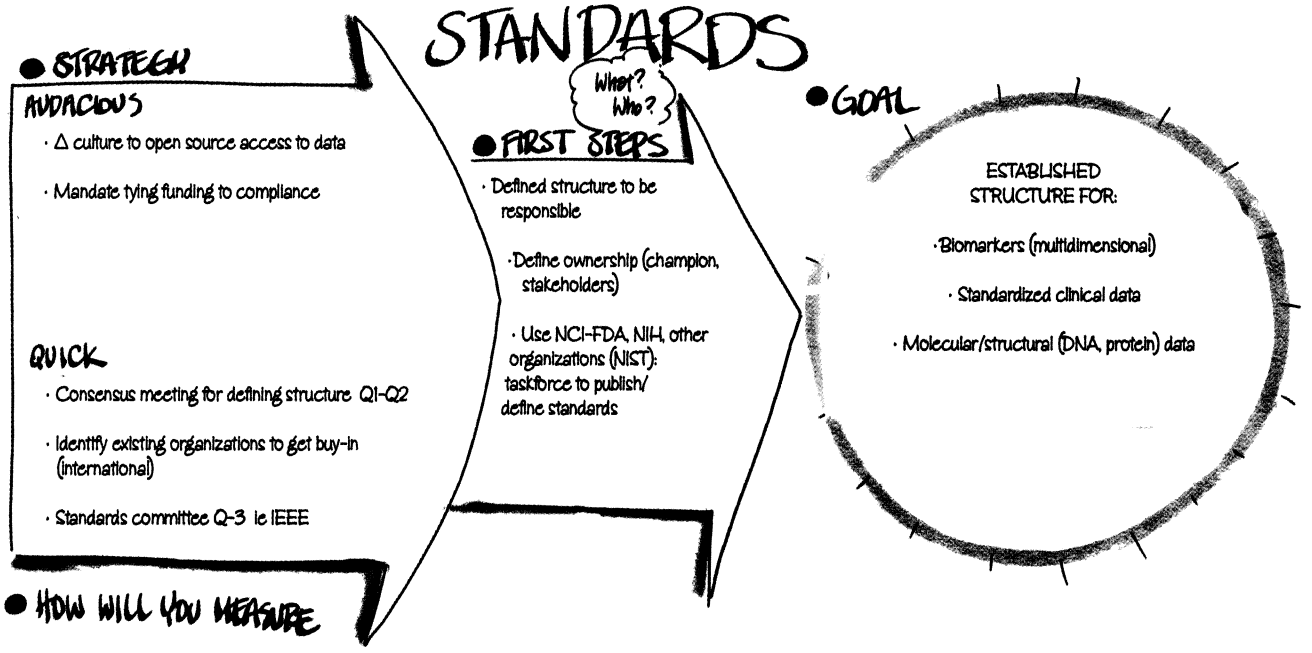
Breakout Groups—Goals and Strategies. Each of the four breakout groups were charged with identifying a goal for the barrier they chose to address, and from that, to create a strategy for reaching that goal. The strategies they developed included





actions they considered easily undertaken as well as those that were more audacious but that would have a disproportionately large impact. Since implementing a strategy depends on taking action, each breakout group also identified a list of concrete steps should be taken in order to seize on the momentum generated by the Roundtable's efforts and begin the necessary transformation of the Nation's advanced biomedical technology development enterprise.





Appendix 4

Leveraging Multi-Sector Technology Development Resources and Capabilities to Accelerate Progress Against Cancer

A National Cancer Institute Roundtable

Meeting Agenda

JANUARY 20, 2004—Day 1

Note: During both meeting days, panels and the overall group will define mission-critical barriers and/or new constructs to set the stage for problem identification and solutions-oriented brainstorming and small group sessions.

7:45 a.m. - 8:30 a.m. *Prefunction Area*

Continental Breakfast

8:30 a.m. - 9:00 a.m. *Grand Ballroom, Section II*

Meeting Background and Expected Outcome
Anna D. Barker, Ph.D.
Deputy Director for Advanced Technologies & Strategic Partnerships
National Cancer Institute, NIH

Goals, Format, Process, and Ground Rules
Robert Mittman, M.S., M.P.P.
Facilitation, Foresight, Strategy

9:00 a.m. - 9:30 a.m.

Advanced Biomedical Technologies in the Conquest of Cancer—A Proposed National Initiative
Andrew von Eschenbach, M.D.
Director, National Cancer Institute, NIH

9:30 a.m. - 11:00 a.m.

Panel 1: The "Contorted" Continuum of Discovering and Developing Advanced Biomedical Technologies

Overview of Technology Development Paradigm
Stephen P.A. Fodor, Ph.D.
Co-Founder, Chairman, and Chief Executive Officer, Affymetrix, Inc.

Basic Research and Discovery (Finding the Great Ideas)
Lee H. Hartwell, Ph.D.
President and Director
Fred Hutchinson Cancer Research Center

Development (Having What It Takes)
David Parkinson, M.D.
Vice President and Head, Clinical Oncology Therapeutic Area
Amgen Inc.

Commercialization and Delivery (Funding the "Winners")
David Morgenthaler
Founding Partner, Morgenthaler Ventures

11:00 a.m. - 11:15 a.m.
Break

11:15 a.m. - 12:30 p.m.
Mission-Critical Barriers to Bringing 21st Century Advanced Health Care Technologies From Concept to Market—Brainstorming Session

12:30 p.m. - 1:40 p.m. *Grand Ballroom, Section I*
Luncheon Presentation
Michael Milken, M.B.A.
Chairman, Center for Accelerating Medical Solutions
Chairman, The Prostate Cancer Foundation

1:40 p.m. - 3:00 p.m.
Panel 2: Models of Regional/State Technology Development That Overcome Barriers and Enhance Advanced Biomedical Technology- Based Economic Growth

Introductions and Overview
Richard Seline
Principal, New Economy Strategies

Philadelphia Model
Frank Baldino, Jr., Ph.D.
Chairman of the Board and Chief Executive Officer, Cephalon, Inc.

North Carolina Model
H. Kim Lyerly, M.D.
Director, Duke Comprehensive Cancer Center

San Diego Model
Ivor Royston, M.D.
Managing Partner, Forward Ventures

3:00 p.m. - 3:15 p.m.
Break

3:15 p.m. - 4:30 p.m.

Panel 3: Innovative Nonprofit Models That Capture Technology and Leverage and Align Philanthropic and Other Resources To Optimize the Development and Commercialization of Advanced Biomedical Technologies (Incremental or Disruptive)

Overview of the Institute for Systems Biology Model
Leroy Hood, M.D., Ph.D.
President, Institute for Systems Biology

Accelerate Brain Cancer Cures (ABC²) Model
Steve Case
Co-Founder, Accelerate Brain Cancer Cure
The Case Foundation

Prostate Cancer Foundation Model
Leslie D. Michelson, J.D.
Vice Chairman and Chief Executive Officer, The Prostate Cancer Foundation

Wisconsin Alumni Research Foundation (WARF) Model
Carl E. Gulbrandsen, Ph.D., J.D.
Managing Director, Wisconsin Alumni Research Foundation

4:30 p.m. - 5:30 p.m.

Prioritizing the Barriers: What Is Really Mission Critical?

6:30 p.m. *The Colonnade*

Reception and Dinner

JANUARY 21, 2004—Day 2

Note: Today will be a "solutions" oriented day focused on approaches that will allow us to optimize and accelerate the discovery, development, and delivery of the advanced biomedical technologies needed to make exponential progress against cancer. Our goal for today is to develop specific recommendations for actions by all sectors that will lead to a new alignment of institutions, initiatives, resources, and teams to optimize and accelerate the discovery, translation, development, and commercialization of advanced health care technologies.

7:45 a.m. - 8:30 a.m. *Prefunction Area*

Continental Breakfast

8:30 a.m. - 9:00 a.m. *Grand Ballroom, Section II*

Review of Day 1 and Goals for Day 2
Robert Mittman, M.S., M.P.P.
Facilitation, Foresight, Strategy

9:00 a.m. - 9:30 a.m.

The Future Isn't What It Used To Be—What It Will Take To Identify and Develop the Needed Disruptive Advanced Biomedical Technologies
G. Steven Burrill
Chief Executive Officer, Burrill & Company

9:30 a.m. - 10:00 a.m.

Panel 4: An "Outside-the-Box" Federal Model To Identify and Accelerate Advanced Technologies—In-Q-Tel

History and Rationale for In-Q-Tel
Richard Seline
Principal, New Economy Strategies

Status and Promise for Cancer
Richard A. Johnson, J.D., M.S.
Senior Partner, Arnold & Porter

The Relevance of the In-Q-Tel Model to Cancer
David Smith
Vice President, Technology Futures, Inc.

10:00 a.m. - 10:15 a.m.

Break

10:15 a.m. - 11:30 a.m.

Group Sessions—Identify Major Barriers and Solutions

11:30 a.m. - 12:15 p.m.

Group Reports

12:15 p.m. - 1:15 p.m. *Grand Ballroom, Section I*

Luncheon Presentation
The Role of HSARPA in Developing Advanced Technologies for Homeland Security
Jane Alexander, Ph.D.
Deputy Director, Homeland Security Advanced Research Projects Agency
U.S. Department of Homeland Security

1:15 p.m. - 2:15 p.m.

Panel 5: Putting the Models to Work: Optimizing and Accelerating the Development of Nanotechnology for Cancer

The Models to Develop Nanotechnology Solutions for Cancer
Scott C. Donnelly
Senior Vice President, Global Research, and Chief Technology Officer
General Electric Company

Nano-Oncology—The "State of the Art" and the NCI Plan
Mauro Ferrari, Ph.D.
Associate Vice President, Health Science Technology and Communications
Associate Director
Dorothy M. Davis Heart and Lung Research Institute

Developing Nanotechnology into Platforms for Diagnosis and Treatment
James R. Heath, Ph.D.
Elizabeth W. Gilloon Professor and Professor of Chemistry
California Institute of Technology

2:15 p.m. - 3:30 p.m.

Panel 6: How Can America's Cancer Centers Serve as Major Vehicles for Capturing, Developing, and Commercializing Advanced Cancer Technologies?

John Mendelsohn, M.D.
President, M. D. Anderson Cancer Center

Jonathan W. Simons, M.D.
Director, Winship Cancer Institute

James K.V. Willson, M.D.
Director, Ireland Cancer Center

3:30 p.m. - 4:00 p.m.

Report Out and Prioritize Final List of Recommendations

4:00 p.m. - 4:30 p.m.

Actions and Next Steps

Andrew von Eschenbach, M.D.
Director, National Cancer Institute, NIH

Anna D. Barker, Ph.D.
Deputy Director for Advanced Technologies & Strategic Partnerships
National Cancer Institute, NIH

Appendix 5

Meeting Participants

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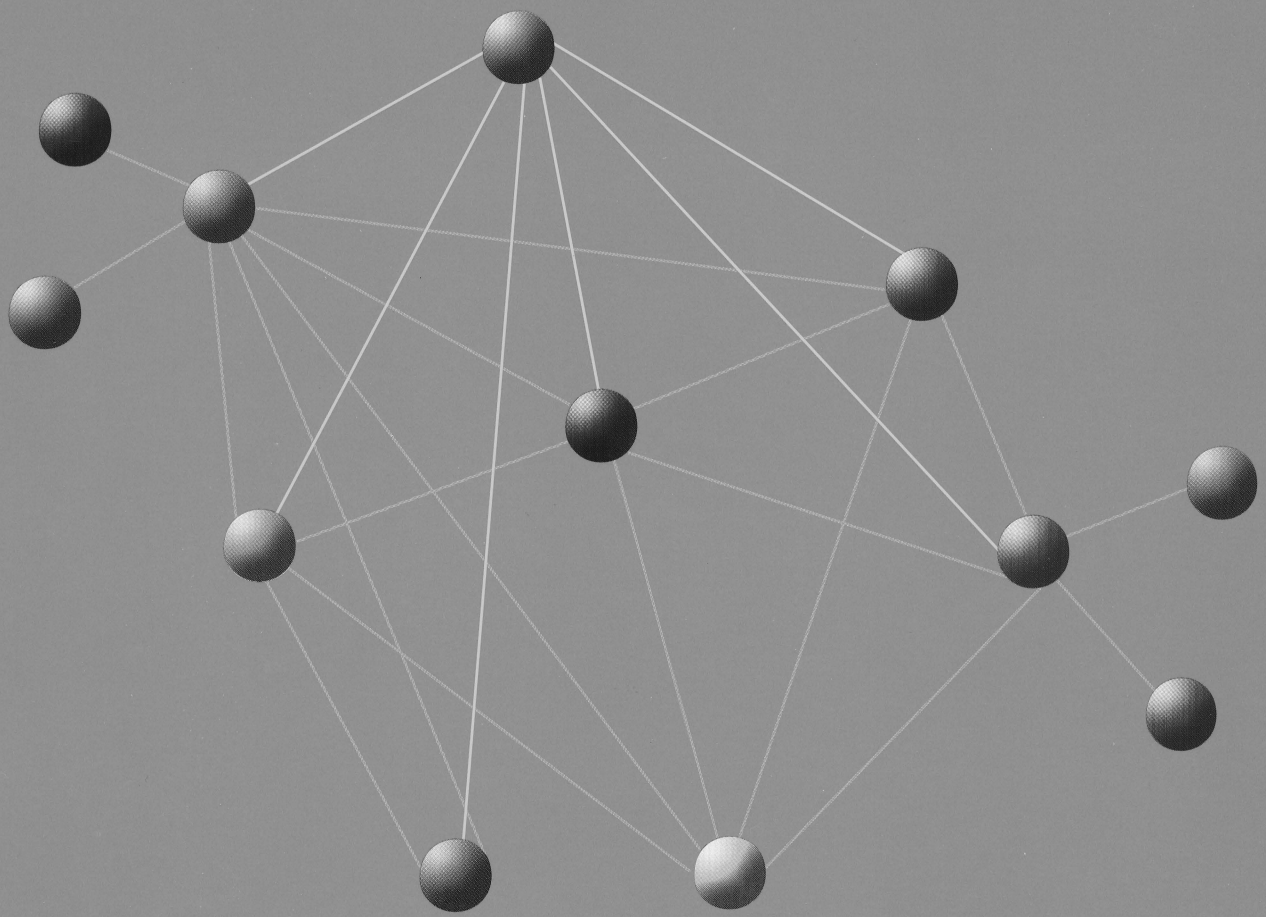




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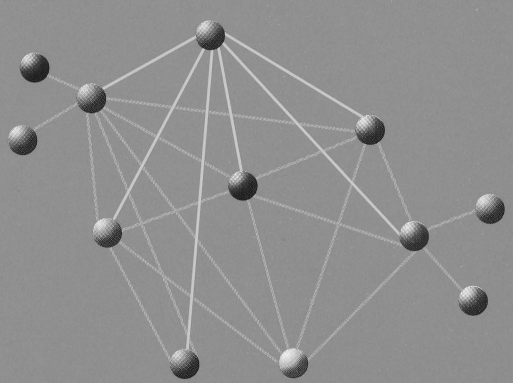
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NATIC

National Advanced Technology Initiative for Cancer



NATIc

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National Advanced Technology Initiative for Cancer Fact Sheet

National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Background

A total of 1.4 million Americans will receive a diagnosis of cancer in 2004 and over 560,000 will die from their disease (1,500/day). With a lifetime cancer risk of 1 in 3 for women and 1 in 2 for men, it is projected that 25 percent of our current population will die from cancer. The economic impact of cancer, currently approximately $180 million per year, is expected to increase as numbers of new cases increase in the next few years due to changing U.S. demographics and the aging of the "baby boomers." The National Cancer Institute (NCI) has challenged the scientific community to transform cancer into a non-lethal disease in the next decade by "eliminating the suffering and death due to cancer."

We stand at a defining moment in our long struggle to conquer cancer. The sequencing of the human genome—coupled with fundamental advances in areas such as immunology, nanotechnology, and bioinformatics–has created an "inflection point" where exponential progress against cancer and other chronic diseases is possible. However, complementing and leveraging basic biomedical research to seize this opportunity requires that we develop a national capability to develop, integrate, and ultimately deploy advanced technologies.

The Proposed Initiative

To accelerate the development of breakthrough diagnostic, therapeutic, and preventive technologies for cancer and other diseases and move strategically toward better health for all Americans, the NCI proposes to create the National Advanced Technology Initiative for Cancer (NATIc). This unprecedented nationwide technology development resource will consist of a virtually integrated and coordinated network of regional "hubs" and "nodes." The 10 or more "hubs" will comprise formally organized and virtually integrated regional clusters of cancer and academic medical centers; State/regional innovation and biotechnology centers; and start-up and other private sector companies.

The Advanced Technology "Hubs"

Each of the hubs will consolidate a critical mass of specialized resources and capabilities, and the integrated NATIc network will represent an unprecedented national advanced technology development enterprise. Examples of potential advanced technology hubs include bioinformatics, systems biology, nanotechnology and biosensors, biomarkers and diagnostics, imaging, drug discovery and development, genome sequence and characterization, and specialized clinical development and trials. A central national hub, to be located at the NCI's Federally Funded Research and Development Center (FFRDC) at Frederick, Maryland, will integrate and coordinate the national network and its specific technology development programs. In addition, the FFRDC Coordinating Hub will provide access to common resources and funding mechanisms for public-private partnerships.

Funding for the NATIc

The NATIc will be funded through a combination of a Federal appropriation of $1.5 billion, $500 million from NCI's operating funds, and $500 million from philanthropy and private sector contributions.

NATIc Operations

Each of the hubs of the NATIc will be responsible for specific deliverables in their area of advanced technology focus. In addition, each of the hubs or consortia of hubs may respond competitively to solve specific advanced technology development problems. These directed technology development programs will require the achievement of milestones. The NATIc will be a magnet for innovative scientists, clinicians, and engineers from the government and academic and private sectors, and each hub will be challenged to attract scientists and engineers who may not currently work in biomedical research.

NATIc Outcomes

Examples of NATIc advanced technology outcomes include:

- Cancer bioinformatics system (Cancer Biomedical Informatics Grid -caBIG) to connect all NATIc advanced technology hubs and the overall cancer search and development enterprise and collect and manage the diagnostic and treatment outcomes for every U.S. cancer patient (caBIG Pilot in process).
- Nationwide, virtually-connected, privacy-protected, high quality biospecimen resource and informatics system to provide clinical materials to support all genomics/proteomics-based cancer research and technology development.
- Nanotechnology diagnostic platform with the capacity to measure a sufficient number of biomarkers to diagnose specific cancers as early as possible, and nanotechnology based biosensors and vectors to detect cellular abnormalities in real time and deliver drugs.
- New generation of advanced cost-effective microchips that will provide the high-throughput capability to profile gene expression for all types of cancer, and develop a "catalogue" of every major cancer genetic abnormality for all cancers (national human cancer genome project).
- Highly connected, "smart" card-supported, national cancer clinical trials system to evaluate targeted diagnostics, therapies, and preventive agents.
- Comprehensive set of biomarkers to define the "signature" of every cancer at the earliest possible point in its evolution, and to specifically stage all established disease; and a systems biology understanding of every abnormal cancer pathway.
- Advanced imaging technology platforms and targeted contrast agents to visualize all functional changes in cancer.
- An advanced national drug-screening platform to support the development of a minimum of 15-20 targeted, safe, highly efficacious chemopreventive and therapeutic drugs for delivery to the right patients at the right time to produce the right outcome for every patient.
- Innovative models for public-private partnerships, new start-up companies and regional high-technology job creation.

NATIc
National Advanced Technology Initiative for Cancer

Advocate for Diagnostics

Although I have never cared for a patient, I find myself today in the strange position of arguing to thousands of the world's top oncologists that we are overlooking the best opportunity to improve cancer outcomes in the shortest possible time. What brings me to this extreme state of hubris stems from the fact that 7 years ago, I left the peaceful environment of the laboratory to become a cancer center director. And, for the first time, I found myself having to answer to patients, physicians, donors and board members: "How are we going to cure cancer in my lifetime?" The only thing worse than having to face you today is to have to answer that question with "I don't know."

In searching for some message of hope for patients and their families, I have come to believe that we could hasten the development of therapeutics and, even more importantly, detect many cancers earlier when they are curable by today's methods if we invested in an organized effort to develop molecular diagnostics as a science.

You no doubt know of people who are pessimistic about our ability to impact cancer outcomes in the short term and others who are optimistic. These extreme views were evident in two articles from major national magazines recently with the *Fortune* article arguing that we are losing the war on cancer while *US News and World Report* emphasized the new survivors enabled by advances in treatment.

Well, count me among the cautious optimists. I am optimistic that we have the knowledge, science and technology to greatly improve outcomes for cancer in a relatively short timeframe, but I am cautious because I don't know whether we have the ability to organize the effort. I hope I can convince you of both of these points—that the science is ready, but organizing the effort is the greatest challenge.

Building on Knowledge

What justifies optimism is our wealth of knowledge about cancer. During the last 40 years, we have achieved an impressive understanding of the molecular fundamentals of cancer. In 1964, when I began my career in cancer research, we knew nothing about the molecular biology of cancer. We now understand that cancer arises in a single cell as a result of genetic changes that alter a number of cellular processes—growth control, immortality, apoptosis, angiogenesis, metastasis—and that these changes are driven by an abnormally high rate of mutation due to defects in cell cycle control and DNA repair. That is an amazing accomplishment in 40 years.

Moreover, new advances are still occurring at an astonishing rate. In just the last few years we have seen the completion of the human genome, providing a catalogue of all human genes; the development of RNA technology that permits the sophisticated genetic analysis of human cells for the first time; and the identification of cancer stem cells. The question of the day is: "Can we now translate this knowledge into improved outcomes for cancer patients?"

Diagnostic Questions

I am going to argue that the shortest path to improving cancer outcomes is improving the science of molecular diagnostics, particularly protein diagnostics. Why molecular diagnostics? To put this in perspective, consider what each new patient you treat wants to know:

Do I have cancer?
What stage is my cancer?
What is the most effective therapy for my cancer?
Is my therapy working?
Have I been cured?
Is my cancer recurring?

These are, of course, diagnostic questions, and the answers to these questions can be found in the molecules of the cancer cells themselves. In the last few years, we have seen enormous strides in molecular diagnostics, primarily at the DNA and RNA level.

A Quiet Revolution

In fact, I would say that there is a quiet revolution occurring in cancer research through improved molecular diagnostics that could completely change the way we treat patients and make it far more effective. Genetic translocations or transcript array profiles are stratifying many organ-specific cancers such as breast, leukemia, lymphoma and sarcoma into different types that have distinctive therapeutic outcomes. For example, whether or not the Myc gene is amplified predicts response to therapy for childhood neuroblastoma. The quantity of Bcr-Abl DNA predicts disease recurrence in chronic myelogenous leukemia long before clinical symptoms recur.

Improved Clinical Trials

The consensus view of how to cure cancer has been through developing new drugs that target the molecular changes in cancer cells. Most basic scientists consider the practical value of their insights as creating targets for new cancer drugs. Indeed, this was my view when I was a laboratory scientist. However, this is too narrow and, by itself, an ineffective view. The hope that more miracle drugs, such as Imantinib, that target molecular changes in cancer cells would cure cancer has been frustrated by the high cost of new drug development, the poor predictive power of animal models, and the complexity of the disease. Although many new drugs are in clinical trials, the success rate has been low, and it is likely to require several target drugs to cure each type of cancer.

Better diagnostics could greatly accelerate new drug development by shortening clinical trials, identifying responsive patients, and revealing toxic side effects. For example, one of the first trials approved with a molecular endpoint is currently under way comparing four treatment arms for chronic myelogenous leukemia. By using

myelogenous leukemia. By using the endpoint of reduction in the DNA marker, Bcr-Abl, Mark Davis and Patrick Brown are conducting a study that would have taken several years to complete but will be reduced to 12 months. Success will be defined as a greater than four log reduction in the Bcr-Abl signal.

If we could routinely follow a patient's response to therapy in real time, both dosing and agent selection could be individualized. A series of agents could be tested on the same patient in a matter of weeks. Combinations could be tested by adding new agents serially to others displaying some efficacy. If a tumor becomes nonresponsive or recurs, a series of different agents could be immediately tested for efficacy.

Molecular diagnostics should be seen as an essential partner to developing new therapeutics. Indeed, Steve Burrill, the guru of the biotech industry, has described the coming era as one of RxDx—emphasizing the necessary role of integrating diagnostics with therapeutics.

Early Diagnosis

However, faster and more successful therapeutic trials are only one benefit to be attained with improved diagnostics and, in fact, not the greatest benefit. With the cost of producing a new drug around a billion dollars, with a decade required for drug approval, and the fact that it will probably take two or three great drugs to cure each type of cancer, even more effective clinical trials through improved diagnostics are not likely to cure cancer in our lifetimes.

I believe the greatest opportunity is to be found with improved diagnostics to detect cancer at an early stage when it is curable with today's methods. For most cancers, 5- and even 10-year survival is often near 90 percent for cancer detected at stage 1 and may be only 10 percent or less for cancer detected at stage 4. We have, of course, known for a long time that if we could detect cancer earlier, we could save more lives. The Pap smear strongly reduces mortality through early detection of cervical cancer as does colonoscopy for colon cancer. We know that early detection can work. What we need are cheap and effective diagnostic tests for more types of cancer. A recent success is the finding that DNA markers are more effective than histologic analysis at detecting progression of Barrett's esophagus to cancer, and, when used in a high-risk population, increases 5-year survival from less than 10 percent to greater than 80 percent.

Risk Assessment

We are all aware of the difficulties inherent in large-scale screening and the potential for overdiagnosis. The recent case of widespread screening for neuroblastoma in children in Canada, which greatly increased the number of invasive treatments but failed to reduce mortality, is a warning. Screening programs will be vastly improved if we can segment the population into smaller groups at increased risk for specific cancers. Success in identifying individuals at increased risk has, of course, been achieved for many cancers through epidemiological studies that identify strong environmental or behavioral risk factors and for rare inherited cancer syndromes.

There is also optimism among some that correlations of inherited genetic variation with disease will reveal common polymorphisms that increase risk of cancer in the larger population. However, Neil Rische has argued persuasively that this approach is unlikely to identify a large fraction of the genetic risk in the population, and studies crossing inbred strains of mice with different risks have generally revealed enormous complexity in the genetic basis of cancer between strains.

However, there is another approach that has received very little attention and could be very effective. It should be possible to identify individuals at risk by phenotypic tests, particularly tests for the effectiveness of DNA repair. Most familial cancer syndromes are due to defects in DNA repair. A study by Scott and Roberts revealed that about 40 percent of breast cancer patients, prior to treatment, exhibit a defect in double strand DNA repair in their white blood cells. We have cell-based and biochemical tests for about 10 different pathways that participate in DNA repair, many of which would likely contribute to cancer risk if defective. More effort could and should be put into risk stratification based on DNA repair capacity.

The Power of Protein Diagnostics

Although we are currently experiencing impressive advances with DNA and RNA-based diagnostics, the greatest power of molecular diagnostics will be found in proteins. Accessing the information in DNA and RNA often requires knowing ahead of time that cancer is present so it can be biopsied and often involves invasive techniques. Diagnostics that can be accessed from easily sampled body fluids, like blood, will be much more useful.

Although methylated DNA and mutated DNA are also promising diagnostic agents in body fluids, proteins carry much more diagnostic information. First, they are more diverse since alternative splicing and more than 100 different posttranslational modifications result in 10 to 100 species of protein from each gene. Moreover, proteins are much more dynamic and reflective of cellular physiology. In one study by Davis and Brown, it was shown that protein phosphorylation can signal the presence of a single double strand break in DNA within seconds to minutes of the activating event.

Yesterday afternoon, a talk by Dr. Soen dramatically illustrated the power of protein diagnostics. In the Davis and Brown laboratories, 2D arrays of proteins have been made that identify first the array of epitopes recognized by circulating T-cells and second the spectrum of cytokines that each T-cell is producing. This type of information is exactly what is needed by the immunotherapy field to understand why some patients show dramatic improvements with immunotherapy and others fail.

Molecular Targeted Imaging

If we can discover protein biomarkers that predict early-stage disease, what then? We will need to know where the cancer is located, how large it is, and whether it is confined. We will need to see it. At present, we can image cancer quite effectively by CT, MRI, ultrasound, or PET. However, we should not think of biomarkers and imaging as independent diagnostic tools.

Each of the major imaging modalities can be greatly enhanced with contrast agents (protein biomarkers as well as other metabolites offer the opportunity not only to see where, but also to see what is going on) to visualize apoptosis, proteolysis, angiogenesis, metastasis—by tagging antibodies with contrast cargo specific for the proteins that are localized and functioning at the site of disease. With informative contrast agents, we can tell which cells are currently repairing DNA damage. We can distinguish cell division from apoptosis in a tumor mass. We can image the characteristically leaky blood vessels in tumors.

The remarkable response of gastrointestinal stromal tumors overexpressing the KIT kinase to the drug Imantinib can be seen within days of treatment through PET imaging of glucose metabolism. Yet, surprisingly, imaging is not used in most clinical trials to achieve rapid and specific assessment of response. This should change.

Basic scientists who have labored to identify the proteins that function in cellular circuits should be aware that their favorite proteins and pathways are more than drug targets—they are the signals that will allow us to visualize and interpret physiology non-invasively. A particularly seminal observation is the discovery from Pat Brown's laboratory that many cancers appear to have activated a wound healing genetic expression program. It is time to unleash the diagnostic and informational content of the protein circuits we have so laboriously identified.

Targeted Therapy

Therapeutic strategies can also benefit directly from an understanding of the proteins that are prominent in each type of cancer. A search for these sentinels of disease would enable a whole industry of new molecularly targeted therapeutic approaches. Many of the broadly toxic agents could become cancer-specific reagents if coupled to antibodies that deliver them specifically to the cancer cells. There is at least one FDA-approved targeted therapy of this type, Myelotarg, which couples an antibody specific for tumor cells with a toxic reagent, calicheamicin, and many more are in development.

State of Proteomics Technology

I hope we can all agree on the enormous potential for protein diagnostics. You may be wondering why, with so much potential, they are not more effectively utilized. Unfortunately, protein diagnostic technology is not only more challenging but also less well developed than that for RNA or DNA. Not only are there many more protein species, an advantage for information content, but they also occur over a much greater dynamic range than RNA or DNA. It is estimated that our blood may contain 1M protein species with abundances that range over at least 10 orders of magnitude. Although we can currently monitor all of the genes and about half of the transcripts on DNA arrays, we have identified only about 0.1 percent of the serum proteins.

However, in the last few years, two advances have vastly improved the potential for protein diagnostics. First are improvements in mass spectrometry, where thousands of peptide features can be displayed, bar-coded by molecular mass, and quantitated with commercially available machines. Second is the human genome information, which provides a limited catalogue of what proteins are present in the human body, permitting efficient identification of proteins displayed by tandem mass spectrometry.

However, since the technology for proteomics accesses less than 0.1 percent of the proteins present in the serum, a systematic approach to protein biomarker discovery requires a "divide and conquer" strategy much as did sequencing the human genome. Like the genome project, it will be necessary to aggregate data across many laboratories. I suspect that the current state of proteomics is, in fact, not that different from the state of DNA sequencing when the scientific community announced its plan to sequence the human genome.

The NCI Early Detection Research Network has done a great job of organizing the studies necessary to validate diagnostic markers, and it is likely that some effective DNA markers will be validated for early detection of cancer. But they are unable to bring the full potential of protein diagnostics to the problem because there has been no robust and effective technology platform for routinely discovering protein biomarkers for cancer.

Need for an Organized Activity

As with the genome project, realizing the potential of protein diagnostics will require a highly organized activity. Industry is not likely to take it on because diagnostics are not considered a lucrative business. But building a robust technology for biomarker discovery is a precompetitive platform that everyone needs and that could be organized as an academic/industry partnership.

We should develop a rigorous science of biomarker discovery. What does that mean? For one, it means starting with mouse models of cancer where the variables can be controlled—where all the animals have identical genotypes, the same environments, the same disease. How will we know the performance capabilities of a technology to discover biomarkers if it is tested only on human samples where none of these variables are controlled and where perfect sensitivity and specificity will likely never exist? With mice, we can easily stage the animals for discovery and then quickly test which markers reveal a therapeutic response. There have been impressive advances from

the NCI mouse consortium over the last few years in creating mouse models of many different human cancers and these provide a great resource for this work.

An effective search for the sentinels of cancer would require a team effort—many laboratories working on the same samples, sharing data, developing standards, and pooling information. It would require an informatics platform that can support these coordinated activities—something that does not now exist in the academic sector. If the human genome sequence had been left to the accumulation of sequences of unknown quality from individual R01-funded laboratories, we would not have a human genome sequence.

Moreover, the discovery of protein biomarkers can be rational. We do not have to sift randomly through hundreds of thousands of proteins in disease versus non-disease looking for rare differences. For example, we could identify empirically the proteins enriched in tumor tissue, in fluids near cancer cells, proteins secreted by human cancer cells in culture or in xenograft capsules. Alternatively, we could look in blood specifically for the nearly 1,000 proteins known to play roles in cancer by a variety of approaches including antibody enrichment. We could make 1,000 antibodies for $10 million—reagents that could allow hundreds of laboratories to search for sentinels of disease in hundreds of cancer types—empowering the entire cancer research community for only 1 percent of the cost of making a single drug. Why aren't we doing it?

These are some of the reasons I say that the science and technology are ready, but that the limiting factor in creating a better future for cancer patients is organizing the coordinated research program that would be necessary. Unfortunately, the current NIH system does not lend itself to funding large, organized projects. Think about how we got the human genome done. It required the creation of a new NIH Institute with a special congressional appropriation. This is not a model we can roll out every time a large project is needed in the biomedical community.

Ending Statement

I have been rather bullish about the potential for protein diagnostics to have a major impact on cancer outcomes. I passionately believe that this is true. But, as scientists, we are all well aware that promising ideas are valuable only if proven to be true, and many of you will remain, appropriately, skeptical. So here is my fallback argument. We are currently investing over $20 billion a year in trying to develop new drugs for cancer, and while there are some promising drugs in current clinical trials, progress has been slow. For a small fraction of that investment and with the will to organize a large community-based effort, we could determine whether diagnostic markers can effectively guide clinical trials and, more importantly, whether they can detect cancer earlier when it can be cured. My argument is that this is the best investment we can make to potentially impact outcomes for this disease in the shortest possible time.

Leland Hartwell, Ph.D., *President and Director of the Fred Hutchinson Cancer Research Center, is the recipient of many national and international scientific awards, including the Nobel Prize. Other honors include the Albert Lasker Basic Medical Research Award, Gairdner Foundation International Award, Brinker International Award for Basic Science, American Cancer Society Medal of Honor and Alfred P. Sloan Award in cancer research. He is a member of the National Academy of Sciences.*

Dr. Hartwell was awarded the 2001 Nobel Prize in Physiology or Medicine for his pioneering work in yeast genetics, and has been studying yeast for more than 35 years. Using the budding yeast that is essential for brewing beer and baking bread, Dr. Hartwell identified many genes that control cell division. Yeast presented many advantages for this work, including its rapid division time, its facile genetic system and its budding shape.

Dr. Hartwell has used yeast to investigate the basis for accurate cellular reproduction and discovered a new class of genes, "checkpoint" genes. These genes encode proteins that notice when mistakes have been made during cellular reproduction and halt cell division so that repair can take place.

The genes that control cell division in yeast subsequently have also been found to control cell division in humans and often to be the site of alteration in cancer. In addition to displaying alterations in cell division, cancer cells, unlike normal cells, also are unstable genetically.

Dr. Hartwell was born October 30, 1939, in Los Angeles. In 1961 he earned a B.S.degree at the California Institute of Technology and in 1964 earned a Ph.D. degree from the Massachusetts Institute of Technology under the mentorship of Dr. Boris Magasanik. He engaged in postdoctoral work at the Salk Institute for Biological Studies from 1964 through 1965 with Dr. Renato Dulbecco. Dr. Hartwell was an Assistant Professor at the University of California, Irvine, from 1965 to 1968. He joined the University of Washington faculty in 1968 and has been a Professor of Genome Sciences there since 1973. In 1996 he joined the faculty of Seattle's Fred Hutchinson Cancer Research Center and one year later, in 1997, attained his current position as President and Director.

Dr. Hartwell lives in Seattle with his wife, Theresa Naujack.

Presented at the meeting of the American Society of Clinical Oncologists (ASCO), New Orleans, June 2004

National Cancer Advisory Board
Ad Hoc Committee on National Advanced Technology Initiative for Cancer

Background

The committee on the National Advanced Biomedical Technology Initiative for cancer (NATIc) was established as an Ad Hoc Working Group of the National Cancer Advisory Board (NCAB) in early 2004. The co-chairs of the Working Group are Dr. Leland Hartwell and Dr. Eric Lander. Dr. Hartwell is President and Director of the Fred Hutchinson Cancer Research Center and recipient of the 2001 Nobel Prize for his pioneering work in yeast genetics. Dr. Lander is Director, Whitehead Center for Genome Research, and Professor, MIT. Dr. Lander was a Rhodes Scholar and has been responsible for developing most of the key tools of modern mammalian genomics. Both are members of the National Academy of Sciences.

The charge to the Working Group included the following: (1) perform a technologic needs analysis with respect to cancer, (2) perform an opportunities analysis to identify technologies that are available and their possible uses, (3) consider possible models for technology and how they can be integrated within the national program, and (4) consider how NCI's efforts in this area can relate to other diseases, other NIH Institutes and Centers, and other agencies.

The first meeting of the Ad Hoc Working Group on NATIc was held on March 24, 2004, in Bethesda. The five Focus Groups held meetings between March and May 2004 and the parent Ad Hoc Working Group reconvened on a teleconference in July to discuss key recommendations. This preliminary report reflects the major recommendations of the parent Ad Hoc Working Group and the five Focus Groups.

The Ad Hoc Working Group and the Focus Groups identified a new call to action from the cancer research community in the area of technology application to the cancer problem. There is a consensus that existing technologies could have a more dramatic impact on cancer outcomes if they were applied more systematically. What is needed is the coordination of research in certain high-impact areas, including the development of data standards, shared reagents and tissues, informatics platforms, and a community of collaboration that permits both the sharing of data and a systematic "divide and conquer" approach. The current individual investigator approach to these issues has not been sufficient to provide the most effective clinical and public health interventions.

In addition, key areas that could benefit immediately from such a coordinated approach and could have a short-term impact on patient outcomes include a systematic analysis of the cancer genome, a systematic search for cancer biomarkers, development of molecularly targeted imaging contrast agents, dissemination and application of RNAi technology, and establishment of a cancer technology exploration initiative. A brief consideration of needs that are common to the effective implementation and application of technology to the cancer field follows. Finally, thoughts related to organizational needs and access and application of these technologies to clinical and public health areas are provided.

Comprehensive Genetic Characterization of Cancer

Opportunity: Cancer begins as a genetic disease. Genetic changes underlie the origin and evolution of all cancers. Cancer is also a finite problem, in that a limited number of genes are altered across the spectrum of cancers. Recent advances in genome technologies have revolutionized our understanding of cancer in a way that has not yet been applied in clinical science. We still organize our research and therapy trials around the organ where cancer occurs (breast, prostate, lung, etc.) rather than around the molecular pathways that are altered. Yet we are learning that a finite number of genetic pathways are altered across the spectrum of cancers and that these pathways are more important for diagnosis, prognosis, and treatment than the organ site in which the cancer develops. Oncogenes like ras and Myc, tumor suppressor genes like p53 and p16, altered DNA repair pathways, and telomerase activation are widespread in tumors. A systematic analysis of genomic changes across cancer sites that identifies all of the major genes, provides assays suitable for clinical use, and reveals the pathways in which these genes operate is both needed and achievable.

Current performance: Current technologies permit characterization of the cancer genome, global gene expression profiles, and epigenetic changes. These technologies have been applied to many cancers, resulting in the identification of numerous cancer subtypes. Major challenges exist. The current information is difficult to gather together because of the lack of quality control standards for collection and presentation of data, lack of protocol standardization, lack of systematic linkage of the results to clinical data, and incomplete application of technologies across cancer types. There has been little research on expression patterns or epigenetic alterations in normal, healthy cells, making it difficult to understand findings in the disease state.

Desired outcome: A key goal is the systematic identification of all chromosomal genetic changes that are factors in cancer, focusing on actual alterations to the DNA molecule including amplifications, deletions, translocations, and point mutations. Technologies such as digital karyotyping, exon sequencing, and genomic mismatch scanning can be applied to identify mutations. Gene expression analysis will serve as a bridge to analysis of phenotypic changes. Finally, there is a need for a systematic identification of recurrent epigenetic changes present in cancer, including changes in DNA methylation and non-DNA elements such as histones.

Requirements:

- Develop "clinical genomics laboratories" to enable transition to clinical implementation.
- Perform genetic and molecular studies in healthy tissues so variations in genes or epigenetic events can be compared with those of cancer patients.
- Develop standards for tissue preparation, protocols, quality control, and data submission.
- Develop guidelines for which genetic alterations merit further functional analysis.

- Coordinate activities to ensure comprehensive analysis and prevent redundant activity.
- Establish a central Web site where all data could be assembled, with public access for all researchers.

Biomarker Discovery

Opportunity: The cancer genome project (described above) will deliver an ability to type cancer by alterations in molecular pathways and will facilitate diagnosis, prognosis, and treatment of cancer. However, each cancer patient can benefit enormously by detecting cancer at its earliest stage and by monitoring its response to therapy in real time. Moreover, clinical trials will be shortened and made more effective if those responding to a new intervention were identified rapidly. Achieving these goals requires noninvasive diagnostics that will be enabled by a catalogue of biomarkers for each type of cancer and by imaging agents targeted to these biomarkers. Most of these biomarkers will be proteins. Thus, there is a need to increase our knowledge of proteins that are altered or abnormally expressed in cancer and those proteins that appear in easily accessible body fluids.

Current performance: Recent advances in mass spectrometry offer one of the best opportunities for current technology for biomarker discovery. However, standards must be identified to facilitate replication of results across laboratories and to permit clinical implementation with other technologies like ELISA tests. Identification of patterns in mass spectrometry is facilitated by tandem mass spectrometry and by the availability of the human genome information, providing a guide to potential proteins. There are, however, still many limitations to the existing technology. The analysis of a single sample requires numerous repetitive analytical cycles to reach a clear conclusion about the identity of specific proteins or peptides. Serum or plasma is believed to contain hundreds of thousands of proteins arrayed over a dynamic range of molecular mass of at least 10 orders of magnitude. While existing technology is adequate for the discovery of abundant biomarkers in cancer tissues or fluids found near a tumor, detecting the same biomarkers in serum or plasma of the circulation is likely to require combining sample enrichment technologies with high-resolution mass spectrometry methods. There has been little attempt to develop standards in the field for tissue collection, sample preparation, internal calibration of instruments, or replication across laboratories or instruments. In some cases, the unique biomarkers in cancer are known to be normal proteins with unusual postranslational modifications, but the ability to identify post-translational modifications by mass spectrometry is primitive.

Desired outcome: A systematic exploration of technology application to complex protein sources is needed to identify the most effective methods for biomarker discovery. This will involve an exploration of tissues, fluids near a tumor site, and plasma with different fractionation methods and ways of combining affinity reagents with analytical methods. Some technology improvements should be encouraged, such as new approaches to high-throughput affinity reagent development. Standard tissue samples, use of mouse cancer models, and standardized reagents would aid data reproduction and comparison. A universally accessible database, algorithms for data analyses, and standardization of data formats are essential.

Requirements:

- Compare and improve methods for fractionation or affinity capture for protein subsets to increase specificity and sensitivity of protein detection.
- Develop quality control and standards for data.
- Catalogue prominent tissue and disease-specific proteins in all common cancers and identify those that are present in easily accessible body fluids.
- Identify those proteins that are present in early-stage disease and those that are signals for therapeutic response.
- Establish centers to conduct data analyses and develop formats for data collection.
- Facilitate the distribution of the capture agents developed.

Molecular Imaging/Probes

Opportunity: Molecularly targeted imaging promises to greatly improve early cancer diagnosis and staging of cancer, reveal therapeutic response within hours to days, and enhance clinical trials by identifying subsets of patients that are likely to respond to a targeted therapy by defining the combination of critical pathways that are essential to the desired clinical outcome. Improved imaging technologies will also increase the sensitivity and specificity of directed needle biopsies and other procedures. Appropriate contrast agents can reveal proliferation, glycolysis, hypoxia, apoptosis, proteolysis, and changes in blood vessels or lymph nodes and many other physiological and biochemical processes. This information will help to stratify patients for treatment and guide the choice of therapeutic intervention.

Current performance: A variety of different imaging modalities in current use such as computed tomography, magnetic resonance imaging, and ultrasound all lend themselves to different forms of molecularly targeted contrast agents. Positron emission tomography and single photon emission computed tomography imaging are noteworthy because many of the isotopes used as tracers for imaging are normal body constituents, and because its enormous sensitivity might lower the barriers to FDA approval, which is a significant problem for new contrast agents. Optical imaging has enormous potential as an in vivo research tool.

Desired outcome: There is a need to develop better and more specific probes with a variety of pharmacological profiles and half-lives, as well as to continue development of "smart" contrast reagents whose signal depends on biochemical activities. Desirable performance enhancements include decreasing the time required to conduct imaging tests to make them more feasible for large-scale trials and clinical implementation, multiplexing contrast agents to compare several biochemical processes at the same time, and developing better transducers to support three-dimensional imaging.

Requirements:

- Integrate the identification of molecular targets and biomarkers with the technologies capable of imaging them in real time.
- Develop effective contrast agents for all biochemical processes that are important in cancer diagnosis.
- Develop effective contrast agents for all biomarkers that are diagnostic of early-stage disease or therapeutic response.
- Educate scientists whose background is a blend of various disciplines (e.g., molecular imaging and cell biology).
- Improve statistical methods to obtain information from complex imaging outputs.
- Facilitate partnerships between industry and academia to facilitate discovery activities in technology development.
- Create a central repository for developing, producing, storing, and calibrating contrast agents and radionuclide probes for use in imaging and diagnostic technologies.
- Create a mechanism for researchers to access and share digital imaging data and algorithms related to imaging. The NCI should have a leadership role in supporting standards for acquiring and analyzing data.
- Integrate imaging as an endpoint into more clinical trials.

Target Validation/RNAi

Opportunity: Many clinical researchers from academia and the pharmaceutical industry are frustrated by the lack of predictive animal models for preclinical validation of drug targets. While the recent development of better mouse models of human cancer may improve the situation, it is likely that mouse studies will never fully mimic human responses. Only in the last year has a solution to target validation in human cells become available with the discovery of gene silencing by RNA interference (RNAi). Creation of RNAi libraries capable of silencing every gene in the human or mouse genome would enable validation of potential therapeutic targets identified in the cancer genome project. Since multiple RNAis can be applied to the same cells, this approach to gene silencing permits studies of gene epistasis and synergy – a common technique for delineating pathways in model organisms. This approach will greatly enhance the understanding of pathways in human cells, benefit the validation of new targets for cancer therapy, and identify the mechanisms of drug resistance and effective drug combinations.

Current performance: Recent refinement of techniques for using RNAi in mammals makes it theoretically possible to inhibit expression of any gene. RNAi libraries targeting more than 9,000 human and more than 5,500 mouse genes have recently been constructed. Although there is still some uncertainty in picking the most effective sequence to target in each gene, algorithms are under development for improving performance and an effective silencer is usually found within two or three attempts. Each clone of the library contains a unique barcode for high-throughput screening and identification of informative RNAis. The human RNAi library has been used to identify new components of the p53 pathway, demonstrating the feasibility of this approach.

Desired outcome: To advance the technology, it will be necessary to create new libraries with regulatable promoters, methods for tissue-specific expression, and new methods to deliver RNAi agents efficiently to cells.

Recommendations:

- Develop RNAi libraries containing several RNAi molecules for each human and mouse gene that is publicly available.
- Establish a database that accumulates information on the effectiveness of these RNAi reagents from investigators who use them.
- Develop methods for more effective delivery of RNAi to cells.
- Develop tissue-specific methods for controlled expression of RNAi.

Cancer Technology Exploration Initiative

Opportunity: There are other extraordinary opportunities for technology to accelerate basic and clinical progress, by providing tools to address crucial needs. Although NCI has successfully undertaken specific efforts, there is no organized program for identifying and seizing such technology-related opportunities. As a result, there can be delays in realizing the potential of technology for cancer.

Current performance: There is a need for continued major investment in the tools for cellular modulation. Such areas hold enormous promise but are still at relatively early stages. These projects are not well suited to the traditional grant process because there is a greater need for prioritization, oversight, and large-scale funding.

Desired outcome: Establish a process whereby, on an ongoing basis, there can be rapid identification of the most pressing opportunities/needs for application-driven technology development and exploration of the structure of appropriate projects to seize these opportunities.

Requirements:

- Determine magnitude of steady-state funding and new funding required for technology development.
- Establish a Cancer Technology Development Committee charged with identifying areas of investment.
- Identify or establish funding mechanisms for work directed toward these goals.

Organizational Needs

Each of the projects identified in the preceding section calls for a systematic and coordinated collaborative approach to providing new knowledge and technology. As such, a number of needs apply to all of the projects. Generally, research is moving to a different model of science that includes larger centers, more centralization, integrated capability, nontraditional job tracks that do not exist in academia, and a very quick cycle for new technologies.

Open access to samples and data is crucial to enable large team projects to go forward. There is a critical need for making available high-quality annotated specimens and conversely preventing archiving materials in a museum. To participate in "living libraries," investigators must agree to share both specimens and data without restriction. There

is also a need for access to full-text research publications and to raw data sets generated by data-rich technologies.

Enhancing bioinformatics capabilities is required to apply many of the advanced technologies described herein to maximum potential. There is currently an informatics gap that causes a lag in researchers' ability to process, analyze, and communicate the data stream being generated by data-rich technologies.

Specific recommendations to move technology forward include:

- Create data standards and statistical methods to analyze highly complex datasets, and standard platforms to share and access data.
- Develop a central and easily accessible database that would eventually contain complete libraries of both DNA and RNA resources.
- Develop informatics tools to support pathway-based and network-based analyses and for conducting haplotype and linkage disequilibrium analyses.
- Develop improved tools for biostatistics and meta-analysis of large datasets.
- Create a Web-based database allowing queries of inventory, risk factors, and clinical data from NCI-sponsored tissue banks. Develop this database into a knowledge bank that gains value as additional information is added; the results of each tissue interrogation should be put back into the database.
- Facilitate the development of a database containing clinical annotation of the genome, proteome, and metabolome including information on prognostics, diagnostics, and therapeutics.
- Develop standardized clinical trial databases including response assessments and molecular profiling.

Setting standards for technology, data collection, and marker validation is required to ensure the reproducibility needed to move advanced technologies toward clinical applications. Moreover, many of the reagent resources and databases described for specific projects may need special portals and additional datasets for application to clinical and public health studies. Their design should include scientists who apply the information as well as those who collect it.

Restructuring clinical trials is needed to make clinical research more adaptable for concurrent dissemination of results as they are obtained from trials. A model for this would be characterized as "smaller and smarter." Future clinical trials could be designed to genotype all patients to identify those who will respond to treatment or give the drug to all patients and genotype the responders. Technologies for future clinical trials will be varied and multimodal. Improved access to standardized archiving of samples, standardized data collection on trials, improved models for cancer therapeutic development, and improved support for team projects specifically for academic/industry partnerships are needed.

Public health-related initiatives include development of practical, affordable, and flexible platforms for the analysis of DNA, RNA, proteins, metabolomics, and epigenetics in large- and small-scale studies targeting all types of cancers. The Public Health Focus Group recommended carrying out quantitative functional pathways analysis that makes measurement of exposure assessment more feasible and develops technologies to convert these platforms into practical assays for clinical implementation in patient care.

Enhanced opportunities for multidisciplinary training are needed at both the pre- and postdoctoral levels in order to ensure that there is a cadre of researchers qualified to conduct research that crosses the boundaries between biology and technology. Examples include training programs for cancer researchers to develop expertise in imaging and vice versa, and more cross-disciplinary training to integrate cancer biology and informatics.

Intellectual property issues should be discussed during the preplanning stage of any large initiative on technology use in cancer research and should encompass background technology as well as technology owned or patented by private industry or universities. Cross-licensing agreements should be developed to cover unique new molecules for probes and diagnostic products that may embody multiple biomarkers. Barriers to sample access may cross content and ownership issues and need to be resolved.

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